10684730 Shalini Sharma

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 NEWS  2         "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27 Source of Registration (SR) information in REGISTRY updated
                 and searchable
 NEWS  4  JAN 27 A new search aid, the Company Name Thesaurus, available in
                 CA/CAplus
 NEWS  5  FEB 05 German (DE) application and patent publication number format
                 changes
 NEWS  6  MAR 03 MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03 MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03 FRANCEPAT now available on STN
 NEWS  9  MAR 29 Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29 WPIFV now available on STN
 NEWS 11  MAR 29 No connect hour charges in WPIFV until May 1, 2004
 NEWS 12  MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 13  APR 26 PROMT: New display field available
 NEWS 14  APR 26 FIPAT/IFIUDB/IFICDB: New super search and display field
                 available
 NEWS 15  APR 26 LITALERT now available on STN
 NEWS 16  APR 27 NLDB: New search and display fields available

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
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DICTIONARY FILE UPDATES:   26 APR 2004  HIGHEST RN 676992-14-6

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http://www.cas.org/ONLINE/DBSS/registryss.html

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L1      STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1                STR
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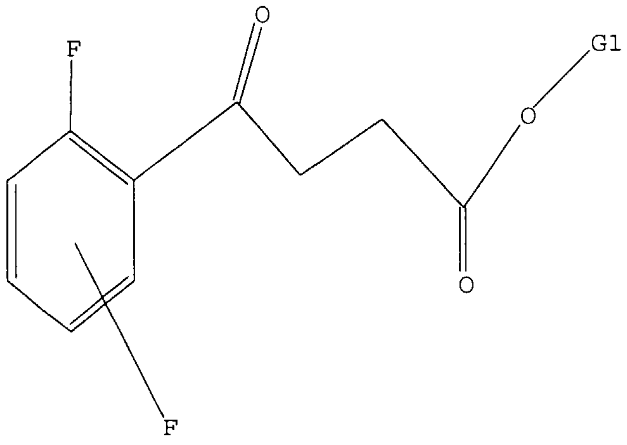

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G1 H,Ak


Structure attributes must be viewed using STN Express query preparation.


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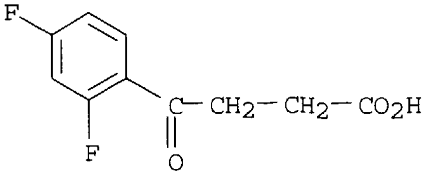
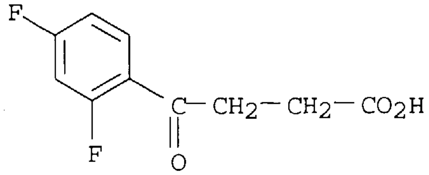


AB Derivs. of the allylamine antimycotic terbinafine with varied substitution at the naphthalene ring system have been prepared, and their antifungal activity has been evaluated. In general, the potency is strongly dependent on the bulkiness of the substituent,. Only hydrogen or in some cases fluorine are tolerated as substituents at positions 2-4 and 6-8 of the naphthalene moiety, whereas 5-substituents may be larger in size (F, Cl, Br, Me). Derivs. with fluorine at positions 3, 5, and 7 or chlorine at position 5 showed enhanced activity against yeasts relative to terbinafine. This increase in sensitivity could be intensified by simultaneous introduction of two fluoro substituents at positions 5 and 7. One compound prepared demonstrated an 8- to 16-fold improved potency against Aspergillus fumigatus, Candida albicans, and Candida parapsilosis.

L7 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:423238 CAPLUS
DN 111:23238
TI New allylamine derivatives, their preparation, and their use as antimycotics
IN Nussbaumer, Peter; Stuetz, Anton; Vyplel, Hermann; Enzersdorf, Maria
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3720317	A1	19881229	DE 1987-3720317	19870619
				DE 1987-3720317	19870619

OS CASREACT 111:23238; MARPAT 111:23238
IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in synthesis of allylnaphthylmethylamine fungicide)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



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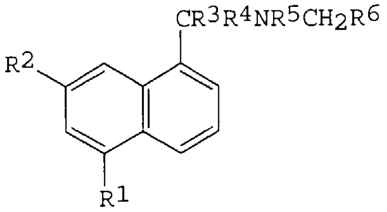

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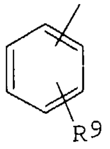

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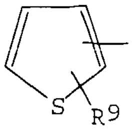

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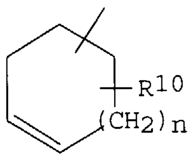

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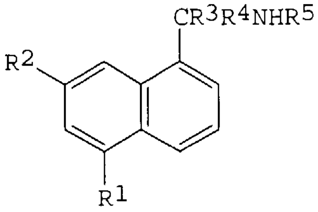
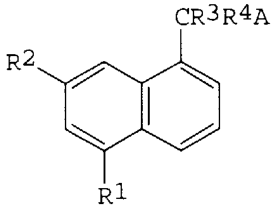


II

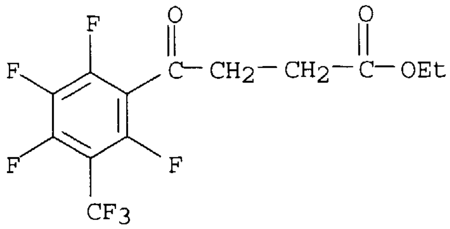


III

AB Naphthalenes I [R1,R2 = H, F; R1 = R2 ≠ H; R3, R4, R5 = H, alkyl; R4, R5 = (CH)2)m ; R5 = CH:CHC.tplbond.CR7, CH:CHCH:CHR7, CH2C.tplbond.CR78 CH:CHR8; R7 = alkyl, cycloalkyl, trialkylsilyl, dialkylphenylsilyl, phenylalkyl, or alkenyl (un)substituted by alkyl, alkoxy, Ph, or halo; R8 = Q, Q1, Q2; R9 = halo, CF3, alkyl, alkyl, H; R10 = H, alkyl; m = 3,4,5; n = 0-2] and their acid salts, useful as medicinal and agrochem. fungicides, were prepared:a) by reaction of amine II with ACH2R6 (A = cleavable group), or b) by reaction of III with R5NH = CH2R6 and optional conversion of the products into acid addition salts. Me3CC.tplbond.CCH:CHCH2Br [(E):(Z) = 3:1] in DMF was added dropwise to (5,7-difluoro-1-naphthylmethyl)methylamine (prepared in 7 steps from 1,3-F2C6H4, AlCl3, and succinic anhydride) and K2CO3 in DMF and the mixture kept 4 h at room temperature to give (E)- and (Z)-I (R1 = R2 = F, R3 = R4 = H, R5 = Me, R6 = CH:CHC.tplbond.CCMe3) (V). The curative dose for V in treating guinea pigs infected with Trichophyton mentagrophytes was 9 + 6 mg/kg in miglyol vs. 9 + 70 mg/kg for griseofulvin.

L7 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:549005 CAPLUS
DN 109:149005
TI Reaction of fluoroorganomagnesium compounds with diethyl dicarboxylates
AU Dormidontov, Yu. P.; Shadrina, L. P.; Belogai, V. D.; Krokhalev, A. M.; Yakhlakova, O. M.
CS USSR
SO Zhurnal Organicheskoi Khimii (1988), 24(1), 107-11
CODEN: ZORKAE; ISSN: 0514-7492
DT Journal
LA Russian
OS CASREACT 109:149005

IT **116547-18-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 116547-18-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,6-tetrafluoro-γ-oxo-5-(trifluoromethyl)-
, ethyl ester (9CI) (CA INDEX NAME)



AB Reactions of fluoroaryl Grignard reagents (e.g., 3-CF3C6H4MgBr, 3-CF3C6F4MgCl, 4-ClC6F4MgCl) with EtO2CXCO2Et (X = null, CMe2, CH2CH2, cyclopropylidene in Et2O were examined At reflux the intermediate ArC(OEt)(OMgX)CO2Et generally lost AcH to give, via ArCH(OMgX)CO2Et, ArCH(OH)CO2Et; at lower temps. the products were ArCOCO2Et.

L7 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:617260 CAPLUS
DN 107:217260
TI Preparation of arylmethylamines as antimycotics and agrochemical fungicides
IN Stuetz, Anton; Nussbaumer, Peter
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 34 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3702039	A1	19870730	DE 1987-3702039	19870124
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				DE 1986-3609123	19860319
				DE 1986-3617635	19860526
				DE 1986-3617637	19860526
	NL 8700083	A	19870817	NL 1987-83	19870115
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				DE 1986-3609123	19860319
				DE 1986-3617635	19860526
				DE 1986-3617637	19860526
	HU 46652	A2	19881128	HU 1987-117	19870115
	HU 211997	B	19960129		
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				DE 1986-3609123	19860319
				DE 1986-3617635	19860526
				DE 1986-3617637	19860526
	CH 672875	A	19900115	CH 1987-244	19870123
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GB 2185980	B2	19900815		
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FR 2597475	A1	19871023	FR 1987-973	19870126
FR 2597475	B1	19910920		
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FI 8700342	A	19870730	FI 1987-342	19870127
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BE 1001550	A5	19891205	BE 1987-51	19870127
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			DE 1986-3617637	19860526
SE 8700328	A	19870730	SE 1987-328	19870128
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			DE 1986-3617635	19860526
			DE 1986-3617637	19860526
DK 8700463	A	19870730	DK 1987-463	19870128
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			DE 1986-3609123	19860319
			DE 1986-3617635	19860526
			DE 1986-3617637	19860526
JP 62201850	A2	19870905	JP 1987-19586	19870128
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IL 81410	A1	19920115	IL 1987-81410	19870128
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AT 8700159	A	19940615	AT 1987-159	19870128
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AU 8768119	A1	19870730	AU 1987-68119	19870129
AU 607694	B2	19910314		
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ZA 8700666	A	19880928	ZA 1987-666	19870129
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     US 4939148          A     19900703          US 1987-8198        19870129
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     CA 1329619          A1    19940517          CA 1987-528508      19870129
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                                                 DE 1986-3617637     19860526
     US 5112851          A     19920512          US 1990-520577      19900508
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                                                 DE 1986-3617637     19860526
                                                 US 1987-8198        19870129
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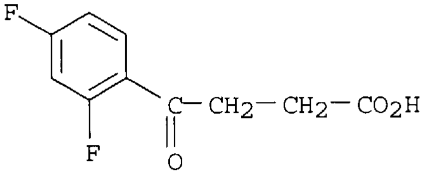
IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)

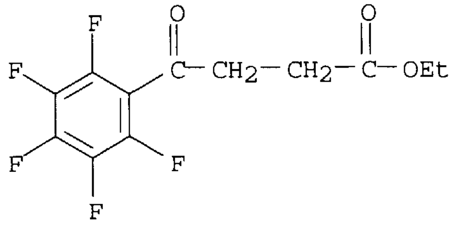


GI For diagram(s), see printed CA Issue.

AB R1R2CHNR3CR4R5R6 [I; R1 = Q-Q5; R2 = H, alkyl; R1R2 = Q6; R2R3 = (CH2)m; R7, R8 = H, halo, CF3, alkyl, alkoxy; R9 = H, halo, alkyl, alkoxy; R10, R11 = H, alkyl, halo, CF3, alkoxy, alkylthio; X = O, S, NH, alkylimino, CH2, OCH2; p = 1-3; s = 3-5; n = 3-6; m = 1-8; in Q3, CH2 may be replaced by O or S; R4, R5 = H, alkyl; R3 = H, cycloalkyl, (halo)alkyl; R6 = Q7-Q10; w = 2-6; Z = O, S, NR3; R12 = aliphatic, cycloalkyl, alkoxy, alkoxycarbonyl, alkylthio, Ph, etc.], were prepared as antimycotics and agrochem. fungicides (no data). A mixture of 4-Me3CC6H4CH2NHMe, K2CO3, and DMF was treated with 1-(bromomethyl)-5,7-difluoronaphthalene and stirred overnight to give N-benzyl-1-naphthalenemethylamine II.

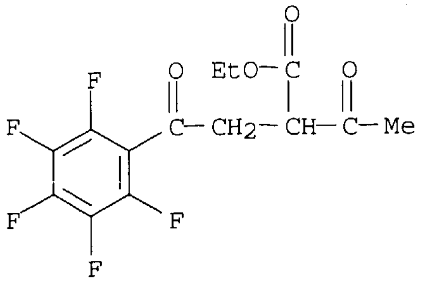
L7 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1981:568741 CAPLUS
DN 95:168741
TI Reaction of pentafluorophenylmagnesium chloride with esters of dibasic

acids
AU Shadrina, L. P.; Dormidontov, Yu. P.
CS Perm. Gos. Univ., Perm, USSR
SO Zhurnal Organicheskoi Khimii (1981), 17(7), 1408-12
CODEN: ZORKAE; ISSN: 0514-7492
DT Journal
LA Russian
OS CASREACT 95:168741
IT **79505-96-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 79505-96-7 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-γ-oxo-, ethyl ester
(9CI) (CA INDEX NAME)



AB C6F5MgCl reacted with Z(CO2Et)2 (Z = bond, Me2C) to give 60-70%
C6F5CH(OH)ZCO2Et (via MeCHO loss) at room temperature and 65-75% C6F5COZCO2Et
at
-20 to -30°. Analogous reaction with EtO2C(CH2)nCO2Et (n = 2-4)
gave 15-22% C6F5CO(CH2)nCO2Et and 12-15% C6F5CO(CH2)nCOC6F5 but no
secondary hydroxy ester. This difference in reactivity correlated with
the pKa values of the corresponding acids, which increased in the stated
order of esters.

L7 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1966:93247 CAPLUS
DN 64:93247
OREF 64:17517e-g
TI Condensation of ω-bromopentafluoroacetophenone with ethyl
sodioacetoacetate
AU Barkhash, V. A.; Andreevskaya, O. I.; Vorozhtsov, N. N., Jr.
CS Inst. Org. Chem., Novosibirsk
SO Doklady Akademii Nauk SSSR (1966), 166(6), 1343-6
CODEN: DANKAS; ISSN: 0002-3264
DT Journal
LA Russian
IT **10019-87-1**, Acetoacetic acid, 2-(2,3,4,5,6-pentafluorophenacyl)-,
ethyl ester
(preparation of)
RN 10019-87-1 CAPLUS
CN Acetoacetic acid, 2-(2,3,4,5,6-pentafluorophenacyl)-, ethyl ester (7CI,
8CI) (CA INDEX NAME)



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GI   For diagram(s), see printed CA Issue.
AB   C6F5Ac brominated in Et2O in the presence of AlCl3 with cooling gave 76.4%
     C6F5COCH2Br, b5 79°,n24.5D 1.4820.  This and 1.3 moles AcCHNaCO2Et
     in Et2O gave after 3 hrs. at reflux 18.5% (CH2COC6F5)2 (I), m.
     97-8.5°; bis(2,4-dinitrophenylhydrazone) m. 231-8°.  The
     filtrate from this gave C6F5COCH2CHAcCO2Et, b3 135-47°, n19.5D
     1.4602, which in cold concentrated H2SO4 1 hr. gave 41.8%
2-methyl-3-carbethoxy-
     5-pentafluorophenylfuran, m. 67-76° (petroleum ether).  I treated
     similarly gave 93.5% 2,5-bis(pentafluorophenyl)furan, m. 117-19.5°
     (EtOH).  I heated 3 hrs. in AcOH with NH4OAc gave 84% 2,5-
     bis(pentafluorophenyl)pyrrole, m. 151-2.5°.  BrCH2COC6F6 heated
     with 2.5% aqueous NaOH 1 hr. gave 83% C6F5Ac.  Reaction of AcCH-NaCO2Et with
     BrCH2Bz gave an undistillable oil which yielded on standing 36.4% II, m.
     103-6° and some III, m. 202-6°.


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     (FILE 'HOME' ENTERED AT 17:12:50 ON 27 APR 2004)

     FILE 'REGISTRY' ENTERED AT 17:13:11 ON 27 APR 2004
L1                STRUCTURE UPLOADED
L2             35 S L1 SSS FULL

     FILE 'MARPAT' ENTERED AT 17:13:44 ON 27 APR 2004
L3             78 S L1 SSS FULL

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                  S L1

     FILE 'REGISTRY' ENTERED AT 17:14:51 ON 27 APR 2004
L4             35 S L1 SSS FULL

     FILE 'CAOLD' ENTERED AT 17:14:52 ON 27 APR 2004
L5              1 S L4 SSS FULL
L6              1 S L2

     FILE 'CAPLUS' ENTERED AT 17:15:48 ON 27 APR 2004
L7             40 S L2
L8             78 S L3
L9             40 S L6
L10             0 S L7 AND 2,6-DIFLUORO
L11             9 S L7 AND DIFLUORO
L12             0 S L8 AND DISLUORO
L13             0 S L8 AND DIFLUORO
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L14           0 S L8 AND 2,6-DIFLUORO
L15           9 S L9 AND DIFLUORO

=> s 17 and agent
L16          12 L7 AND AGENT

=> s 18 and agent
L17          41 L8 AND AGENT

=> s 19 and agent
L18          12 L9 AND AGENT

=> s 116 and 117 and 118
L19           2 L16 AND L17 AND L18

=> d 119 fbib hitstr abs total

L19  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:97391  CAPLUS
DN   138:137324
TI   Preparation of phenylpropionic acid derivatives as α4 integrin
     inhibitors
IN   Chiba, Akira; Sagi, Kazuyuki; Yoshimura, Toshihiko; Okuzumi, Tatsuya;
     Izawa, Hiroyuki; Murata, Masahiro
PA   Ajinomoto Co., Inc., Japan
SO   PCT Int. Appl., 57 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2003010135      A1   20030206      WO 2002-JP7543   20020725
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                               JP 2001-225749 A 20010726
OS   MARPAT 138:137324
IT   493004-41-4P, 4-(2,6-Difluorophenyl)-2-[4-(1-methyl-2,4-dioxo-
     1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxobutanoic acid
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of phenylpropionic acid derivs. as α4 integrin inhibitors
        for prevention or treatment of α4 integrin-participating various
        diseases)
RN   493004-41-4  CAPLUS
CN   Benzenebutanoic acid, α-[[4-(1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-
     quinazolinyl)phenyl]methyl]-2,6-difluoro-γ-oxo- (9CI)  (CA INDEX
     NAME)
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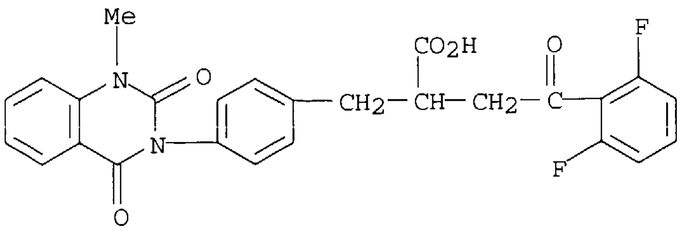
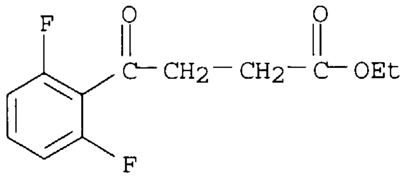


IT **493004-53-8P**, 4-(2,6-Difluorophenyl)-4-oxobutanoic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)

RN 493004-53-8 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, ethyl ester (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylpropionic acid derivs. represented by the general formula (I) [wherein A = Q-Q4, (un)substituted Ph, NR1-Z, NR1-CO-Z, NR1-SO2-Z, NR1-CONH-Z, NR1-C(:S)-NH-Z; wherein Z = (un)substituted Ph, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N;
R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl,

or heteroaryl; E = CO, CHOH; G-G1 = $CH-CH_2$, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO_2] are prepared These derivs. exhibit $\alpha 4$ integrin inhibiting activity and are useful as therapeutic or preventive **agents** for various diseases in which $\alpha 4$ integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac_2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac_2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28% 2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III). Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at 70° for 2 h and then at 70° for 11 h in the presence of Et_3N gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was methylated by MeI in the presence of K_2CO_3 in DMF for 1 h to quant. give IV (R = R24 = Me, X = H). Saponification of the latter compound with aqueous LiOH in aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R = Me, R24 = X = H). IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl) in vitro inhibited the binding of vascular cellular adhesion mol.-1 (VCAM-1) to human B cell lymphoma cell expressing integrin $\alpha 4\beta 7$ with IC_{50} of ≤ 20 to < 100 μmol/L and ≤ 0.9 μmol/L, resp.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:964135 CAPLUS
DN **138:24543**
TI Preparation of benzyloxyphenyloxobutyrates and related compounds for the treatment of metabolic disorders
IN Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA Wellstat Therapeutics Corporation, USA
SO PCT Int. Appl., 242 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002100341	A2	20021219	WO 2002-US18388	20020612

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

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          BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                              US 2001-297282PP 20010612
     US 2003149107     A1   20030807          US 2002-167839   20020612
                                              US 2001-297282PP 20010612
     US 2004077896     A1   20040422          US 2003-684644   20031014
                                              US 2001-297282PP 20010612
                                              US 2002-167839 A320020612
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OS MARPAT 138:24543

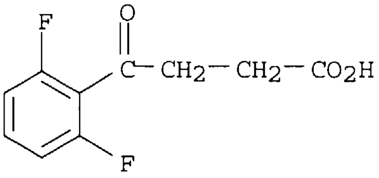
IT **478162-62-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzyloxyphenyloxobutyrates and related compds. for treatment of metabolic disorders)

RN 478162-62-8 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



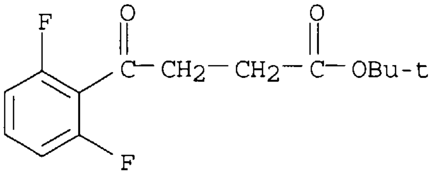
IT **478163-14-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzyloxyphenyloxobutyrates and related compds. for treatment of metabolic disorders)

RN 478163-14-3 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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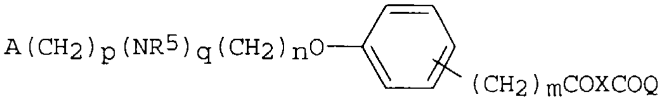

I

AB Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = H, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 =

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     Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2,
     Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other =
     H, alkyl], were prepared  Thus, 4-(2-fluorobenzyloxy)acetophenone (preparation
     given) in THF and DMPU was treated with a solution of Li
     bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu
     bromoacetate was added followed by stirring for an addnl. 10 min and
     warming to room temperature for 4 h to give tert-Bu 4-[4-(2-
     fluorobenzyloxy)phenyl]-4-oxobutyrate.  The latter was stirred with
     CF3CO2H in CH2Cl2 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric
     acid.  Tested I showed antidiabetic activity in a variety of tests.  I are
     useful in treatment of various metabolic disorders such as insulin
     resistance syndrome, diabetes, hyperlipidemia, fatty liver disease,
     cachexia, obesity, atherosclerosis and arteriosclerosis.


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=> d his

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                S L1

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L5              1 S L4 SSS FULL
L6              1 S L2

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L7             40 S L2
L8             78 S L3
L9             40 S L6
L10             0 S L7 AND 2,6-DIFLUORO
L11             9 S L7 AND DIFLUORO
L12             0 S L8 AND DISLUORO
L13             0 S L8 AND DIFLUORO
L14             0 S L8 AND 2,6-DIFLUORO
L15             9 S L9 AND DIFLUORO
L16            12 S L7 AND AGENT
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L18            12 S L9 AND AGENT
L19             2 S L16 AND L17 AND L18

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=> s 18 and biological
L21            9 L8 AND BIOLOGICAL
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L22           5 L9 AND BIOLOGICAL

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L21  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:279562  CAPLUS
DN   138:304276
TI   Preparation of pyrazoles as glycine transporter protein inhibitors for the
     treatment of neurodegenerative diseases
PA   Merck Patent G.m.b.H., Germany; Yamanouchi Pharmaceutical Co.
SO   Ger. Offen., 62 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
FAN.CNT 1
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PI   DE 10149370        A1   20030410       DE 2001-10149370 20011006
     WO 2003031435      A1   20030417       WO 2002-EP10172  20020911
     WO 2003031435      C1   20030515
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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                                            DE 2001-10149370A 20011006
OS   MARPAT 138:304276
GI
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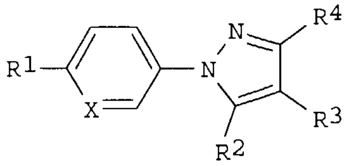

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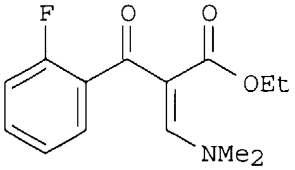

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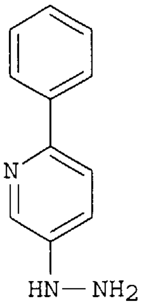
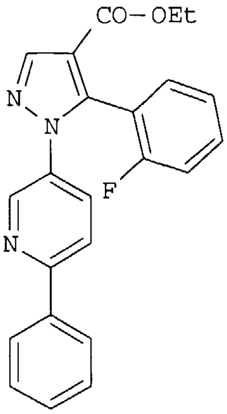


III



IV

AB Title compds. I [X = CH, N; R1 = H, A, halo, etc.; R2 = Ph, p-chlorophenyl; R3, R4 = H, (CH2)nCO2R5, CHO, etc.; R5 = H, A; A = alkyl, alkenyl, alkoxyalkyl, etc.; n = 0-5] and their pharmaceutically acceptable salts were prepared For example, condensation of enamine II e.g., prepared from 1,1-dimethoxy-N,N-dimethylmethanamine and 2-fluoro-β-oxo-benzenepropanoic acid Et ester, and aryl hydrazine III, e.g., prepared from 2-chloro-5-nitropyridine in 3-steps, provided pyrazole IV (no yield provided). In glycine transporter protein inhibition studies, approx. 71-examples of compds. I exhibited IC50 values ranging from 0.15 - 8.7 μM, e.g., the IC50 value of pyrazole IV = 2.5 μM. Compds. I are claimed useful for the treatment of schizophrenia, depression, dementia, etc.

L21 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:97391 CAPLUS
DN **138:137324**
TI Preparation of phenylpropionic acid derivatives as α4 integrin inhibitors
IN Chiba, Akira; Sagi, Kazuyuki; Yoshimura, Toshihiko; Okuzumi, Tatsuya; Izawa, Hiroyuki; Murata, Masahiro
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

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     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2003010135        A1   20030206      WO 2002-JP7543   20020725
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG
JP 2001-225749 A 20010726

OS MARPAT 138:137324
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylpropionic acid derivs. represented by the general formula (I) [wherein A = Q-Q4, (un)substituted Ph, NR1-Z, NR1-CO-Z, NR1-SO2-Z, NR1-CONH-Z, NR1-C(:S)-NH-Z; wherein Z = (un)substituted Ph, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N;

R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl, or heteroaryl; E = CO, CHOH; G-G1 = CH-CH2, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These derivs. exhibit α4 integrin inhibiting activity and are useful as therapeutic or preventive agents for various diseases in which α4 integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28% 2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III). Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at 70° for 2 h and then at 70° for 11 h in the presence of Et3N gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was methylated by MeI in the presence of K2CO3 in DMF for 1 h to quant. give IV (R = R24 = Me, X = H). Saponification of the latter compound with aqueous LiOH in aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R = Me, R24 = X = H). IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl) in vitro inhibited the binding of vascular cellular adhesion mol.-1 (VCAM-1) to human B cell lymphoma cell expressing integrin $\alpha 4\beta 7$ with IC50 of ≤ 20 to <100 μmol/L and ≤ 0.9 μmol/L, resp.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:964135 CAPLUS
DN **138:24543**
TI Preparation of benzyloxyphenyloxobutyrates and related compounds for the treatment of metabolic disorders
IN Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA Wellstat Therapeutics Corporation, USA
SO PCT Int. Appl., 242 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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     PATENT NO.          KIND  DATE           APPLICATION NO.   DATE
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PI   WO 2002100341        A2   20021219       WO 2002-US18388   20020612
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
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                                              US 2001-297282PP 20010612
     US 2003149107        A1   20030807       US 2002-167839   20020612
                                              US 2001-297282PP 20010612
     US 2004077896        A1   20040422       US 2003-684644   20031014
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OS MARPAT 138:24543
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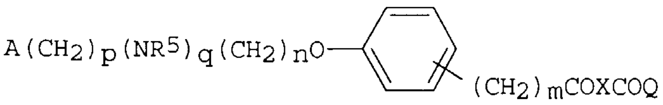

I

AB Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = H, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 = Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2, Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other = H, alkyl], were prepared Thus, 4-(2-fluorobenzyloxy)acetophenone (preparation

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     given) in THF and DMPU was treated with a solution of Li
     bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu
     bromoacetate was added followed by stirring for an addnl. 10 min and
     warming to room temperature for 4 h to give tert-Bu 4-[4-(2-
     fluorobenzyloxy)phenyl]-4-oxobutyrate.  The latter was stirred with
     CF3CO2H in CH2Cl2 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric
     acid.  Tested I showed antidiabetic activity in a variety of tests.  I are
     useful in treatment of various metabolic disorders such as insulin
     resistance syndrome, diabetes, hyperlipidemia, fatty liver disease,
     cachexia, obesity, atherosclerosis and arteriosclerosis.

L21  ANSWER 4 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:539523  CAPLUS
DN   137:88466
TI   Isoflavones in combination with lipid-regulating agents for regulation of
     lipids and/or bone density, and compositions therefor
IN   Husband, Alan James
PA   Novogen Research Pty. Ltd., Australia
SO   PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2002055072      A1   20020718       WO 2002-AU42     20020116
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                            AU 2001-2554   A 20010116
     EP 1351682         A1   20031015       EP 2002-709886   20020116
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                            AU 2001-2554   A 20010116
                                            WO 2002-AU42   W 20020116
     NO 2003003134      A    20030903       NO 2003-3134     20030708
                                            AU 2001-2554   A 20010116
                                            WO 2002-AU42   W 20020116
OS   MARPAT 137:88466
AB   A method and compns. are provided for regulating bone d. and/or
     circulating lipid levels in a subject which are based on the combined
     administration of at least one isoflavone, or functional derivative,
equivalent,
     or analog thereof, and at least one lipid-regulating drug.  The method and
     compns. are applicable to the beneficial alteration of blood lipoprotein
     levels, the improvement of vascular compliance, the decrease in the
     propensity of thrombogenic events, the reduction in the risk of vascular
     disease, coronary heart disease, and arteriosclerosis, and to the
     treatment or prevention of osteoporosis.
RE.CNT  7      THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L21   ANSWER 5 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    2001:617966  CAPLUS
DN    135:180619
TI    Preparation of diaryl compounds as inhibitors of retinoic acid metabolism.
IN    Nicholls, Paul Joseph; Smith, Harold John; Greer, Valierie Patricia;
      Ahmadi, Masoud; Mason, Peter
PA    University College Cardiff Consultants Limited, UK
SO    PCT Int. Appl., 127 pp.
      CODEN: PIXXD2
DT    Patent
LA    English
FAN.CNT 1
      PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
      ---------------   ----  --------      ---------------   --------
PI    WO 2001060781      A2   20010823      WO 2001-GB686     20010219
      WO 2001060781      A3   20020314
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                GB 2000-3671    A 20000217
OS    MARPAT 135:180619
GI
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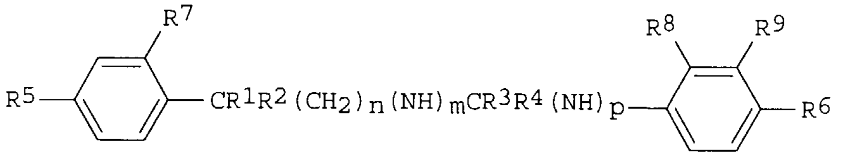

I

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AB    Use of title compds. [I; R1, R2 = H, CH2OH, OH, halo, alkoxycarbonyl; R1R2
      = O, OCH2CH2O; R3 = H; R4 = OH, OT; T = CO2R10, COR10; R10 = alkyl,
      aralkyl, diaralkyl, aryl; R3R4 = O; R5, R6 = H, halo, NH2, alkylamino,
      dialkylamino, NO2; R7-R9 = H, halo; n = 0, 1; m, p = 0, 1; with provisos]
      for therapy is claimed.  Thus, 4-nitrotoluene and 2,4-dichlorobenzaldehyde
      were stirred with NaOH in DMF for 2 h at room temperature to give 59.6%
      1-(2,4-dichlorophenyl)-2-(4-nitrophenyl)-1-ethanol.  The latter was heated
      with concentrate HNO3 on a boiling water bath for 2.5 h to give 55.9%
      1-(2,4-dichlorophenyl)-2-(4-nitrophenyl)-1,2-ethanedione.  This at 100
      μM gave 83.1% inhibition of retinoic acid metabolizing cytochrome P
      450.

L21   ANSWER 6 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    2000:98493  CAPLUS
DN    132:132323
TI    Diketoacid derivatives as inhibitors of viral polymerases
IN    Altamura, Sergio; Tomei, Licia; Koch, Uwe; Neuner, Philippe Jean
      Siegfried; Summa, Vincenzo
PA    Istituto Di Ricerche Di Biologia Molecolare P Angeletti S.p.A., Italy;
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     Nicholls, Kathryn Margaret
SO   PCT Int. Appl., 105 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
     ---------------     ----  --------       ---------------  --------
PI   WO 2000006529        A1   20000210       WO 1999-GB2446   19990727
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
     CA 2338490           AA   20000210       CA 1999-2338490  19990727
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
                                              WO 1999-GB2446 W 19990727
     AU 9950595           A1   20000221       AU 1999-50595    19990727
     AU 756627            B2   20030116
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
                                              WO 1999-GB2446 W 19990727
     EP 1100763           A1   20010523       EP 1999-934986   19990727
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
                                              WO 1999-GB2446 W 19990727
     JP 2003525200        T2   20030826       JP 2000-562336   19990727
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
                                              WO 1999-GB2446 W 19990727
     US 6492423           B1   20021210       US 2001-744795   20010126
                                              GB 1998-16358  A 19980727
                                              US 1998-96528P P 19980813
                                              WO 1999-GB2446 W 19990727
     US 2003207922        A1   20031106       US 2002-238246   20020910
                                              GB 1998-16358  A 19980727
                                              WO 1999-GB2446 W 19990727
                                              US 2001-744795 A320010126
OS   MARPAT 132:132323
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AB Diketoacids (RCOCH2COCO2H) are useful as inhibitors of viral polymerases, in particular hepatitis C virus RNA dependent RNA polymerase (HCV RdRp), hepatitis B virus polymerase (HBV pol) and reverse transcriptase of human immunodeficiency virus (HIV RT). The group R may be broadly chosen and is an organic moiety which contains 2 to 24 carbon atoms and includes an optionally cyclic or heterocyclic group in which the atom directly bonded to the adjacent carbonyl in the diketoacid is part of the ring structure. A compound of present invention which is effective in the inhibition of one of the RNA-dependent polymerases tested may not necessarily be as effective in inhibiting the other RNA-dependent polymerases. Generally,

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     the most active inhibitors of HCV RdRp contained a Ph ring attached to the
     diketo acid, whereas the HIV RT inhibitors contained a furanyl group and
     those of HBV polymerase a thiophene group.
RE.CNT  5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21  ANSWER 7 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1996:746318  CAPLUS
DN   126:16248
TI   Purification and characterization of the human pro-apoptotic cysteine
     proteinase, apopain, and its modulation by peptidyl inhibitors or gene
     therapy
IN   Miller, Douglas K.; Thornberry, Nancy A.; Nicholson, Donald W.; Ali,
     Ambereen; Vaillancourt, John P.
PA   Merck and Co., Inc., USA; Merck Frosst Canada Inc.; Miller, Douglas K.;
     Thornberry, Nancy A.; Nicholson, Donald W.; Ali, Ambereen; Vaillancourt,
     John P.
SO   PCT Int. Appl., 83 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9633268         A1   19961024      WO 1996-US5282   19960417
         W:  CA, JP, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                           US 1995-426557   19950421
     CA 2218679         AA   19961024      CA 1996-2218679  19960417
                                           US 1995-426557   19950421
     EP 822983          A1   19980211      EP 1996-913801   19960417
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
                                           US 1995-426557   19950421
                                           WO 1996-US5282   19960417
     JP 11504209        T2   19990420      JP 1996-531866   19960417
                                           US 1995-426557   19950421
                                           WO 1996-US5282   19960417
OS   MARPAT 126:16248
AB   The present invention is directed to an isolated and purified enzyme
     designated apopain, methods of using apopain to screen for compds. which
     modulate the activity of apopain, and compds. identified by the screens.
     Thus, a poly(ADP-ribose) polymerase cleavage activity (apopain) was
     detected in progressively apoptotic human osteosarcoma cells.  Apopain was
     purified and structural anal. showed it to comprise 2 subunits (p17 and
     p12) proteolytically processed from the 32-kDa CPP32 precursor by cleavage
     at the Asp28-Ser29 and Asp175-Ser176 positions.  A synthetic DNA mol.
     encoding full-length apopain is prepared from the purified enzyme.  The
     synthetic apopain-encoding DNA is formulated so as to optimize expression
     in a variety of recombinant hosts.  The DNA clones produce recombinant
     full-length apopain and derivs. thereof.  Purified native apopain and
     recombinant apopain are useful for identifying modulators of apopain
     activity and hence modifier of pathol. conditions related to the
     pro-inflammatory or pro-apoptotic effects of apopain.  Thus, the
     tetrapeptide aldehyde inhibitor Ac-YVAD-CHO acts with a Ki of <1 nM,
     making it among the most potent peptide aldehydes known for a cysteine
     proteinase.  The synthesis of Ac-YVAD-CHO is described in detail, and can
     be generally applied for the synthesis of other peptidyl inhibitors.
     Apopain antisense mols. are useful for therapeutically reducing or
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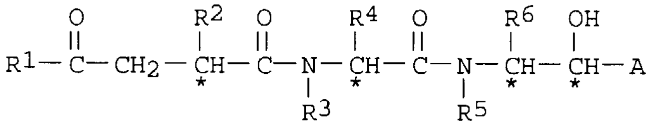
eliminating the pro-inflammatory or pro-apoptotic effects of apopain, whereas gene transplantation or gene therapy with apopain is useful for enhancing the pro-inflammatory or pro-apoptotic effects of apopain. These therapies are beneficial in the treatment of immune, proliferative and degenerative diseases including, but not limited to, immune deficiency syndromes (such as AIDS), autoimmune diseases, pathogenic infections, cardiovascular and neurol. injury, alopecia, aging, cancer, Parkinson's disease and Alzheimer's disease.

L21 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:931615 CAPLUS
DN **124:146860**
TI Preparation of renin-inhibiting dipeptide derivatives as antihypertensive agents
IN Albright, Jay D.; Howell, Charles F.
PA American Cyanamid Co., USA
SO U.S., 27 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5459131	A	19951017	US 1991-669717	19910315
				US 1991-669717	19910315

OS MARPAT 124:146860
GI


$$R^1-\overset{O}{\overset{\|}{C}}-CH_2-\overset{R^2}{\underset{*}{CH}}-\overset{O}{\overset{\|}{C}}-\underset{R^3}{N}-\overset{R^4}{\underset{*}{CH}}-\overset{O}{\overset{\|}{C}}-\underset{R^5}{N}-\overset{R^6}{\underset{*}{CH}}-\overset{OH}{\underset{*}{CH}}-A$$

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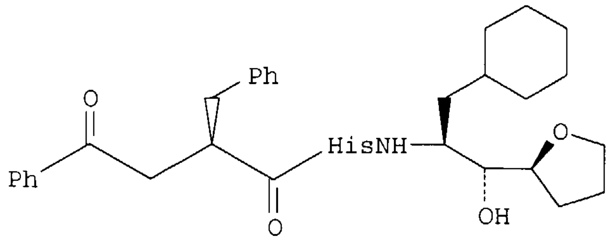

II

AB Renin inhibiting compds. of the formula I [R1 = e.g., (un)substituted Ph, furanyl, thienyl; R2 = e.g., phenylmethyl, cyclohexylmethyl, lower alkyl (C1-C6), 1-naphthalenylmethyl, (benzo[b]thien-3-yl)methyl, (benzo[b]thien-2-yl)methyl, (3-benzofuranyl)methyl, (2-benzofuranyl)methyl; R3 = H or Me; R4 = e.g., alkyl(C1-C8), phenylmethyl, cyclohexylmethyl, 4-imidazolylmethyl, (4-imidazolyl)CH2X, X-alkyl (C1-C8), (C2)nN[loweralkyl(C1-C3)]2, (CH2)nNH alkyl (C1-C3), X-cyclohexyl, (CH2)n X-alkyl (C1-C3), XCH2CH2N[alkyl(C1-C3)]2 (where X is O or S and n is an integer from 1 to 4); R5 is hydrogen or methyl; R6 = e.g., alkyl(C1-C6),

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     phenylmethyl, cyclohexylmethyl; A = e.g., (un)substituted furanyl,
     thienyl] are claimed which inhibit the substrate-cleaving action of renin,
     as well as pharmaceutical compns. containing these compds., processes for
     producing the compds., and methods of treating hypertension which employ
     the novel renin inhibitors.  Thus, e.g., peptide coupling of
     (R)-γ-oxo-α-(phenylmethyl)benzenebutanoic acid
     (N-methylmorpholine, iso-Bu chloroformate) with 2-[[2-amino-3-(1H-imidazol-
     4-yl)-1-oxopropyl]amino]-4,7-anhydro-1-cyclohexyl-1,2,5,6-tetradeoxy-L-
     arabino-heptitol (preparation given) afforded dipeptide analog II which
     exhibited an IC50 = 7 + 10-11 M for renin inhibition.

L21  ANSWER 9 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1995:886111  CAPLUS
DN   123:286027
TI   Preparation of (phenylalkyl)imidazole H3-receptor antagonists
IN   Aslanian, Robert G.; Green, Michael J.; Shih, Neng-Yang
PA   Schering Corp., USA
SO   PCT Int. Appl., 53 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9514007         A1   19950526      WO 1994-US12717  19941110
         W:  AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR,
             KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ,
             TT, UA, US, UZ, VN
         RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
             MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
             TD, TG
                                       US 1993-153231 A 19931115
     CA 2176557         AA   19950526      CA 1994-2176557  19941110
                                       US 1993-153231 A 19931115
     AU 9511712         A1   19950606      AU 1995-11712    19941110
     AU 693142          B2   19980625
                                       US 1993-153231 A 19931115
                                       WO 1994-US12717W 19941110
     EP 729459          A1   19960904      EP 1995-902442   19941110
     EP 729459          B1   20030312
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
                                       US 1993-153231 A 19931115
                                       WO 1994-US12717W 19941110
     HU 74386           A2   19961230      HU 1996-1282     19941110
                                       US 1993-153231 A 19931115
     JP 09505298        T2   19970527      JP 1994-514478   19941110
                                       US 1993-153231 A 19931115
                                       WO 1994-US12717W 19941110
     NZ 330898          A    20000128      NZ 1994-330898   19941110
                                       US 1993-153231 A 19931115
     AT 234290          E    20030315      AT 1995-902442   19941110
                                       US 1993-153231 A 19931115
                                       WO 1994-US12717W 19941110
     ES 2188649         T3   20030701      ES 1995-902442   19941110
                                       US 1993-153231 A 19931115
PATENT FAMILY INFORMATION:
FAN  1996:725348
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     --------------- ---- --------         -------------- --------
PI   US 5578616       A    19961126         US 1995-469941   19950606
                                            US 1993-153231 B219931115
     CA 2176557       AA   19950526         CA 1994-2176557  19941110
                                            US 1993-153231 A 19931115
     HU 74386         A2   19961230         HU 1996-1282     19941110
                                            US 1993-153231 A 19931115
     NZ 330898        A    20000128         NZ 1994-330898   19941110
                                            US 1993-153231 A 19931115
     ES 2188649       T3   20030701         ES 1995-902442   19941110
                                            US 1993-153231 A 19931115
OS   MARPAT 123:286027
GI
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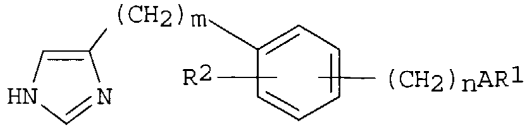

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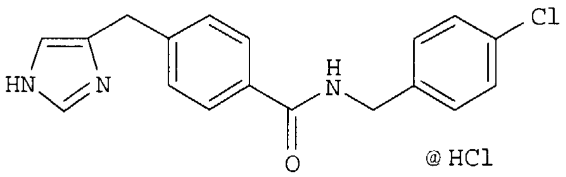

II

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AB   The title compds. [I; A = (un)substituted O2CNH, O2C, (un)substituted
     NHCONH, (un)substituted NHCO, (un)substituted NH, O, CO2, etc.; R1 = H,
     alkyl, (un)substituted aryl, (un)substituted heterocyclic; R2 = H,
     halogen, alkenyl, alkynyl, CF3, etc.; m = 1-3], useful as H3-receptor
     antagonists in the treatment of allergies, inflammation, CNS diseases,
     etc., are prepared and I-containing formulations presented.  Thus,
     N-[(4-chlorophenyl)methyl]-4-(1H-imidazol-4-ylmethyl)benzamide HCl, II,
     was prepared and demonstrated a 61% inhibition of the binding of tritiated
     methylhistamine to guinea pig brain-derived H3 receptors at 2 µg/mL.


=> s l22 fbib hitstr abs total
MISSING OPERATOR L22 FBIB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d l22 fbib hitstr abs total

L22  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:841823  CAPLUS
DN   140:87057
TI   Benzyl vinylogous amide substituted aryldihydropyridazinones and
     aryldimethylpyrazolones as potent and selective PDE3B inhibitors
AU   Edmondson, Scott D.; Mastracchio, Anthony; He, Jiafang; Chung, Christine
     C.; Forrest, Michael J.; Hofsess, Scott; MacIntyre, Euan; Metzger, Joseph;
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O'Connor, Naphtali; Patel, Kajal; Tong, Xinchun; Tota, Michael R.; Van der Ploeg, Lex H. T.; Varnerin, Jeff P.; Fisher, Michael H.; Wyvratt, Matthew J.; Weber, Ann E.; Parmee, Emma R.

CS Department of Medicinal Chemistry, Merck & Co., Inc., Rahway, NJ, 07065, USA

SO Bioorganic & Medicinal Chemistry Letters (2003), 13(22), 3983-3987
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science B.V.

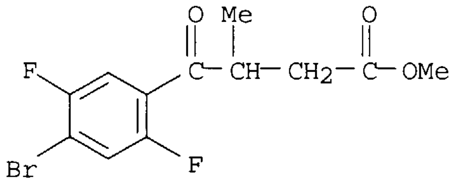
DT Journal

LA English

IT **644984-85-0P 644985-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)

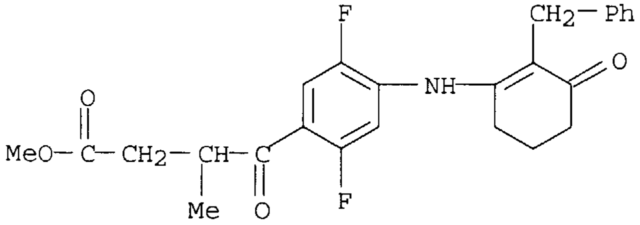
RN 644984-85-0 CAPLUS

CN Benzenebutanoic acid, 4-bromo-2,5-difluoro-β-methyl-γ-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 644985-01-3 CAPLUS

CN Benzenebutanoic acid, 2,5-difluoro-β-methyl-γ-oxo-4-[[3-oxo-2-(phenylmethyl)-1-cyclohexen-1-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)



AB Aryldihydropyridazinones and aryldimethylpyrazolones with 2-benzyl vinylogous amide substituents have been identified as potent PDE3B subtype selective inhibitors. One dihydropyridazinone (PDE3B IC50=0.19 nM, 3A IC50=1.3 nM) was selected for in vivo evaluation of lipolysis induction, metabolic rate increase, and cardiovascular effects.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:97391 CAPLUS

DN 138:137324

TI Preparation of phenylpropionic acid derivatives as α4 integrin inhibitors

IN Chiba, Akira; Sagi, Kazuyuki; Yoshimura, Toshihiko; Okuzumi, Tatsuya; Izawa, Hiroyuki; Murata, Masahiro
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

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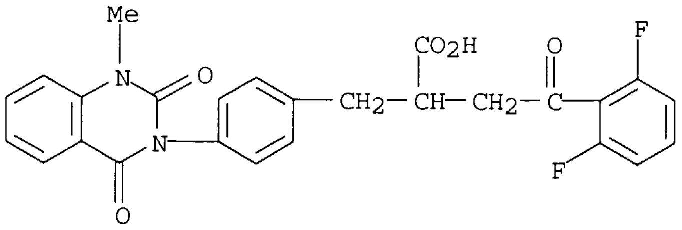
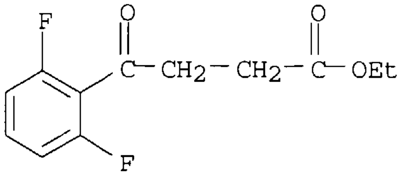
     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ---------------     ----  --------      ---------------   --------
PI   WO 2003010135        A1   20030206      WO 2002-JP7543    20020725
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                             JP 2001-225749 A 20010726
```

OS MARPAT 138:137324
IT **493004-41-4P**, 4-(2,6-Difluorophenyl)-2-[4-(1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxobutanoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)
RN 493004-41-4 CAPLUS
CN Benzenebutanoic acid, α-[[4-(1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)phenyl]methyl]-2,6-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



IT **493004-53-8P**, 4-(2,6-Difluorophenyl)-4-oxobutanoic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)
RN 493004-53-8 CAPLUS
CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, ethyl ester (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylpropionic acid derivs. represented by the general formula (I) [wherein A = Q-Q4, (un)substituted Ph, NR1-Z, NR1-CO-Z, NR1-SO2-Z, NR1-CONH-Z, NR1-C(:S)-NH-Z; wherein Z = (un)substituted Ph, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N;

R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl, or heteroaryl; E = CO, CHOH; G-G1 = CH-CH2, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These derivs. exhibit α4 integrin inhibiting activity and are useful as therapeutic or preventive agents for various diseases in which α4 integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28% 2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III). Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at 70° for 2 h and then at 70° for 11 h in the presence of Et3N gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was methylated by MeI in the presence of K2CO3 in DMF for 1 h to quant. give

```
     IV (R = R24 = Me, X = H).  Saponification of the latter compound with aqueous
LiOH in
     aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R =
Me,
     R24 = X = H).  IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl)
     in vitro inhibited the binding of vascular cellular adhesion mol.-1
     (VCAM-1) to human B cell lymphoma cell expressing integrin α4β7
     with IC50 of ≤20 to <100 μmol/L and ≤0.9 μmol/L, resp.
RE.CNT  12     THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22  ANSWER 3 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:964135  CAPLUS
DN   138:24543
TI   Preparation of benzyloxyphenyloxobutyrates and related compounds for the
     treatment of metabolic disorders
IN   Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA   Wellstat Therapeutics Corporation, USA
SO   PCT Int. Appl., 242 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2002100341     A2   20021219      WO 2002-US18388  20020612
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                      US 2001-297282PP 20010612
     US 2003149107     A1   20030807      US 2002-167839   20020612
                                      US 2001-297282PP 20010612
     US 2004077896     A1   20040422      US 2003-684644   20031014
                                      US 2001-297282PP 20010612
                                      US 2002-167839 A320020612
OS   MARPAT 138:24543
IT   478162-62-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzyloxyphenyloxobutyrates and related compds. for
        treatment of metabolic disorders)
RN   478162-62-8  CAPLUS
CN   Benzenebutanoic acid, 2,6-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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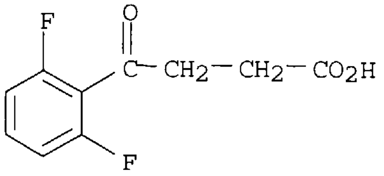
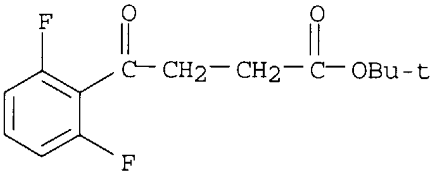


IT **478163-14-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzyloxyphenyloxobutyrates and related compds. for treatment of metabolic disorders)

RN 478163-14-3 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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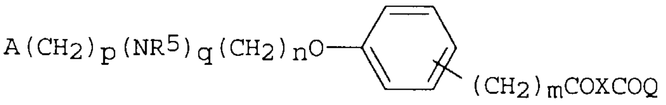

I

AB Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = H, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 = Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2, Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other = H, alkyl], were prepared Thus, 4-(2-fluorobenzyloxy)acetophenone (preparation given) in THF and DMPU was treated with a solution of Li bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu bromoacetate was added followed by stirring for an addnl. 10 min and warming to room temperature for 4 h to give tert-Bu 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyrate. The latter was stirred with CF3CO2H in CH2Cl2 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric acid. Tested I showed antidiabetic activity in a variety of tests. I are useful in treatment of various metabolic disorders such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis.

L22 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:50386 CAPLUS
DN 126:152347
TI The measurement of molecular diversity: a three-dimensional approach

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L7   ANSWER 20 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1997:780649  CAPLUS
DN   128:48214
TI   Preparation of 3,5-diphenyl-2(5H)-furanone derivatives as nonpeptide
     endothelin I antagonists
IN   Berryman, Kent Alan; Doherty, Annette Marian; Edmunds, Jeremy John; Patt,
     William Chester; Plummer, Mark Stephen; Repine, Joseph Thomas
PA   Warner-Lambert Co., USA
SO   U.S., 120 pp., Cont.-in-part of U.S. Ser. No. 278,882, abandoned.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   US 5691373          A    19971125      US 1995-384083   19950206
                                            US 1993-109751   19930819
                                            US 1994-217578   19940324
                                            US 1994-278882   19940726
     CA 2165567          AA   19950223      CA 1994-2165567  19940809
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     HU 74179            A2   19961128      HU 1996-365      19940809
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                                            US 1994-217578   19940324
                                            US 1994-278882   19940726
     ZA 9406265          A    19960219      ZA 1994-6265     19940818
                                            US 1993-109751   19930819
     US 6017916          A    20000125      US 1997-787423   19970122
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PATENT FAMILY INFORMATION:
FAN  1995:896100
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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PI   WO 9505376          A1   19950223      WO 1994-US9091   19940809
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         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                            US 1993-109751   19930819
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                                            WO 1994-US9091   19940809
     EP 714391           A1   19960605      EP 1994-925831   19940809
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
                                            US 1993-109751   19930819
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			US 1994-217578	19940324
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			WO 1994-US9091	19940809
HU 74179	A2	19961128	HU 1996-365	19940809
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			WO 1994-US9091	19940809
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FI 9600671	A	19960419	FI 1996-671	19960214
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			US 1994-278882	19940726
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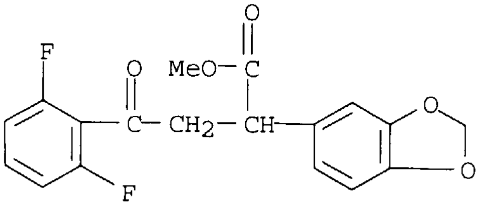
NO 9600629	A	19960216	NO 1996-629	19960216
			US 1993-109751	19930819
			US 1994-217578	19940324
			US 1994-278882	19940726
			WO 1994-US9091	19940809

OS MARPAT 128:48214
IT **169803-96-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diphenylfuranone derivs. as nonpeptide endothelin I antagonists for disease treatment)
RN 169803-96-7 CAPLUS
CN 1,3-Benzodioxole-5-acetic acid, α-[2-(2,6-difluorophenyl)-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)



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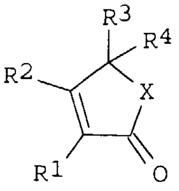

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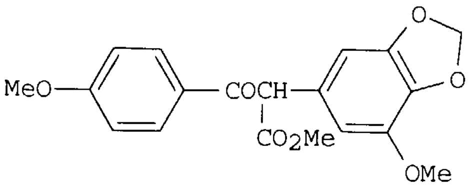

II

AB Novel nonpeptide antagonists of endothelin I represented by formula [I; R1 = (un)substituted C3-12 cycloalkyl, Ph substituted with 1-5 substituents, naphthyl or heteroaryl optionally substituted with 1-5 substituents; R2 = C1-12 linear or branched alkyl, C3-12 linear or branched cycloalkyl, aryl optionally substituted with 1-5 substituents, heteroaryl optionally substituted with 1-3 substituents; R3 = (un)substituted C1-12 linear or branched alkyl, (un)substituted C3-12 cycloalkyl, aryl optionally substituted with 1-5 substituents, heteroaryl optionally substituted with 1-3 substituents; R4 = OH, OR5, (CH2)nOR5; wherein R5 = (un)substituted C1-7 alkyl; X = O, S] or tautomeric open chain keto-acids forms thereof or pharmaceutically acceptable salt thereof are prepared Also described are pharmaceutical compns. of the above compds., which are useful in treating elevated levels of endothelin, acute and chronic renal failure, hypertension, myocardial infarction, myocardial ischemia, cerebral vasospasm, cerebral ischemia, cerebral infarction, cirrhosis, septic shock, congestive heart failure, endotoxic shock, subarachnoid hemorrhage, arrhythmia, asthma, preeclampsia, atherosclerotic disorders including Raynaud's disease and restenosis, angina, cancer, pulmonary hypertension, ischemic disease, gastric mucosal damage, hemorrhagic shock, ischemic bowel disease, stroke, benign prostatic hyperplasia (BPH), and diabetes. Thus, Me 2-benzoyl-2-phenylacetate derivative (II) and 3,4,5-trimethoxybenzladehyde were refluxed in the presence of NaOMe in MeOH for 18 h and the solution was treated with AcOH and refluxed an addnl. 72 h, followed by saponification of the product with 1N aqueous NaOH and acidification to give 28% I (X = O, R1 = Q, R2 = 3,4,5-trimethoxyphenyl, R3 = 4-methoxyphenyl, R4 = OH). The latter compound in vitro showed an antagonism of endothelin I-stimulated vasoconstriction in the rabbit femoral artery and sarafotoxin 6c-stimulated vasoconstriction in the rabbit pulmonary artery with pA2 values of 0.00025 and 0.34, resp.

L7 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:265845 CAPLUS
DN 126:277438
TI (Pentafluorobenzoyl)pyruvate ester and its derivatives in reactions with o-aminophenol
AU Saloutin, V. I.; Perevalov, S. G.; Skryabina, Z. E.
CS Inst. Org. Sint., Ural. Otd. RAN, Yekaterinburg, 620219, Russia
SO Zhurnal Organicheskoi Khimii (1996), 32(9), 1386-1389
CODEN: ZORKAE; ISSN: 0514-7492
PB Nauka
DT Journal
LA Russian
IT **161037-54-3**, Ethyl (pentafluorobenzoyl)pyruvate
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation with aminophenol)
RN 161037-54-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

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                  and searchable
 NEWS  4  JAN 27  A new search aid, the Company Name Thesaurus, available in
                  CA/CAplus
 NEWS  5  FEB 05  German (DE) application and patent publication number format
                  changes
 NEWS  6  MAR 03  MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03  FRANCEPAT now available on STN
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 NEWS 10  MAR 29  WPIFV now available on STN
 NEWS 11  MAR 29  No connect hour charges in WPIFV until May 1, 2004
 NEWS 12  MAR 29  New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 13  APR 26  PROMT: New display field available
 NEWS 14  APR 26  FIPAT/IFIUDB/IFICDB: New super search and display field
                  available
 NEWS 15  APR 26  LITALERT now available on STN
 NEWS 16  APR 27  NLDB: New search and display fields available

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
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COST IN U.S. DOLLARS                                 SINCE FILE     TOTAL
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                                                    ENTRY    SESSION
FULL ESTIMATED COST                                  0.21       0.21

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DICTIONARY FILE UPDATES:  27 APR 2004  HIGHEST RN 677274-15-6

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L1      STRUCTURE UPLOADED

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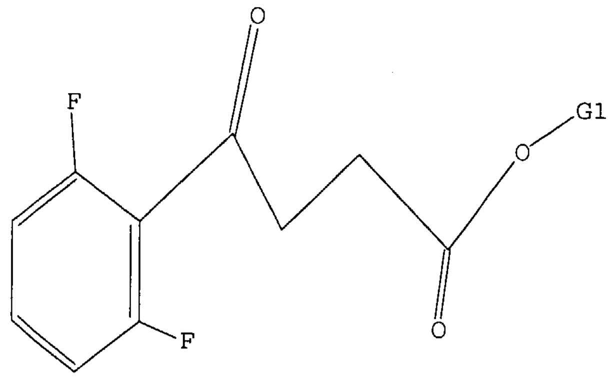

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G1 H,Ak


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FULL SCREEN SEARCH COMPLETED -     152 TO ITERATE
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100.0% PROCESSED     152 ITERATIONS                            24 ANSWERS
SEARCH TIME: 00.00.01

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FULL ESTIMATED COST                                        155.42     155.63

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US    6709645 23 MAR 2004
DE   10335606 11 MAR 2004
EP    1403278 31 MAR 2004
JP 2004099560 02 APR 2004
WO 2004024934 25 MAR 2004

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higher limits.

=> s l1 sss full
FULL SEARCH INITIATED 16:19:33 FILE 'MARPAT'
FULL SCREEN SEARCH COMPLETED -  11804 TO ITERATE

 53.6% PROCESSED    6324 ITERATIONS                            38 ANSWERS

 81.5% PROCESSED    9621 ITERATIONS                            55 ANSWERS

 94.9% PROCESSED   11202 ITERATIONS                            62 ANSWERS

100.0% PROCESSED   11804 ITERATIONS                            69 ANSWERS
SEARCH TIME: 00.01.04

L3            69 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                   SINCE FILE      TOTAL
                                                            ENTRY    SESSION
FULL ESTIMATED COST                                        109.84     265.47

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FILE COVERS 1907 - 28 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 27 Apr 2004  (20040427/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


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     FILE 'CAPLUS' ENTERED AT 16:20:43 ON 28 APR 2004

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=> s l3
L5            69 L3

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EXPRESSION CONTAINS ANSWER SETS CREATED IN MORE THAN ONE
ADDITIONAL FILE
The query entered contains answer sets from two different
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File crossover can only be done from one file to another.

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L6             2 L4 AND L5

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L6   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:97391  CAPLUS
DN   138:137324
TI   Preparation of phenylpropionic acid derivatives as α4 integrin
     inhibitors
IN   Chiba, Akira; Sagi, Kazuyuki; Yoshimura, Toshihiko; Okuzumi, Tatsuya;
     Izawa, Hiroyuki; Murata, Masahiro
PA   Ajinomoto Co., Inc., Japan
SO   PCT Int. Appl., 57 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
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FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003010135	A1	20030206	WO 2002-JP7543	20020725

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

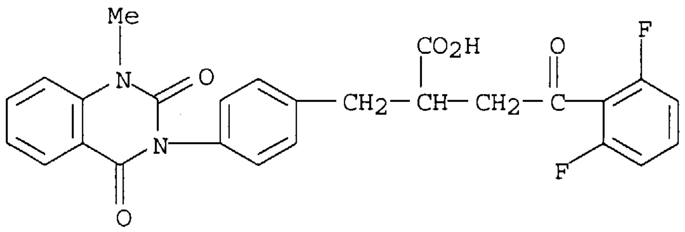
JP 2001-225749 A 20010726

OS MARPAT 138:137324

IT **493004-41-4P**, 4-(2,6-Difluorophenyl)-2-[4-(1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxobutanoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)

RN 493004-41-4 CAPLUS

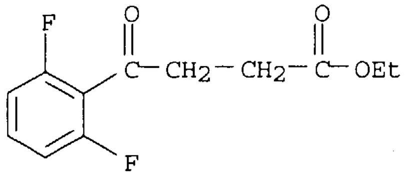
CN Benzenebutanoic acid, α-[[4-(1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)phenyl]methyl]-2,6-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



IT **493004-53-8P**, 4-(2,6-Difluorophenyl)-4-oxobutanoic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)

RN 493004-53-8 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, ethyl ester (9CI) (CA INDEX NAME)



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylpropionic acid derivs. represented by the general formula (I) [wherein A = Q-Q4, (un)substituted Ph, NR1-Z, NR1-CO-Z, NR1-SO2-Z, NR1-CONH-Z, NR1-C(:S)-NH-Z; wherein Z = (un)substituted Ph, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N;

R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl, or heteroaryl; E = CO, CHOH; G-G1 = CH-CH2, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These derivs. exhibit α4 integrin inhibiting activity and are useful as therapeutic or preventive agents for various diseases in which α4 integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28% 2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III). Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at 70° for 2 h and then at 70° for 11 h in the presence of Et3N gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was methylated by MeI in the presence of K2CO3 in DMF for 1 h to quant. give IV (R = R24 = Me, X = H). Saponification of the latter compound with aqueous LiOH in

```
     aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R =
Me,
     R24 = X = H).  IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl)
     in vitro inhibited the binding of vascular cellular adhesion mol.-1
     (VCAM-1) to human B cell lymphoma cell expressing integrin α4β7
     with IC50 of ≤20 to <100 μmol/L and ≤0.9 μmol/L, resp.
RE.CNT  12     THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:964135  CAPLUS
DN   138:24543
TI   Preparation of benzyloxyphenyloxobutyrates and related compounds for the
     treatment of metabolic disorders
IN   Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA   Wellstat Therapeutics Corporation, USA
SO   PCT Int. Appl., 242 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   WO 2002100341      A2   20021219       WO 2002-US18388  20020612
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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             TJ, TM
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     US 2003149107      A1   20030807       US 2002-167839   20020612
                                            US 2001-297282PP 20010612
     US 2004077896      A1   20040422       US 2003-684644   20031014
                                            US 2001-297282PP 20010612
                                            US 2002-167839 A320020612
OS   MARPAT 138:24543
IT   478162-62-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzyloxyphenyloxobutyrates and related compds. for
        treatment of metabolic disorders)
RN   478162-62-8  CAPLUS
CN   Benzenebutanoic acid, 2,6-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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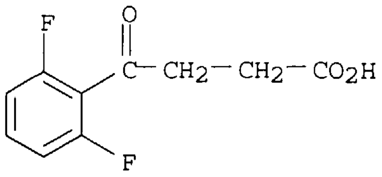
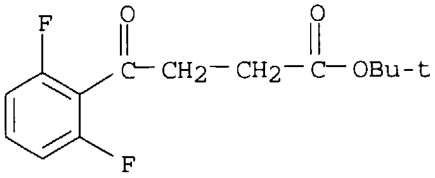


IT **478163-14-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzyloxyphenyloxobutyrates and related compds. for treatment of metabolic disorders)
RN 478163-14-3 CAPLUS
CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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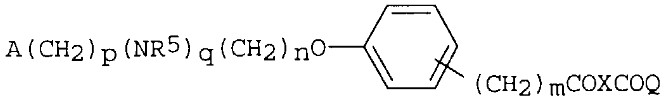

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AB Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = H, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 = Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2, Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other = H, alkyl], were prepared Thus, 4-(2-fluorobenzyloxy)acetophenone (preparation given) in THF and DMPU was treated with a solution of Li bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu bromoacetate was added followed by stirring for an addnl. 10 min and warming to room temperature for 4 h to give tert-Bu 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyrate. The latter was stirred with CF3CO2H in CH2Cl2 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric acid. Tested I showed antidiabetic activity in a variety of tests. I are useful in treatment of various metabolic disorders such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis.

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     (FILE 'HOME' ENTERED AT 16:18:32 ON 28 APR 2004)

     FILE 'REGISTRY' ENTERED AT 16:18:43 ON 28 APR 2004
L1                STRUCTURE UPLOADED
L2            24 S L1 SSS FULL

     FILE 'MARPAT' ENTERED AT 16:19:26 ON 28 APR 2004
L3            69 S L1 SSS FULL
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cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N; R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl, or heteroaryl; E = CO, CHOH; G-G1 = CH-CH2, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These derivs. exhibit α4 integrin inhibiting activity and are useful as therapeutic or preventive agents for various diseases in which α4 integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28% 2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III). Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at 70° for 2 h and then at 70° for 11 h in the presence of Et3N gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was methylated by MeI in the presence of K2CO3 in DMF for 1 h to quant. give IV (R = R24 = Me, X = H). Saponification of the latter compound with aqueous LiOH in aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R = Me, R24 = X = H). IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl) in vitro inhibited the binding of vascular cellular adhesion mol.-1 (VCAM-1) to human B cell lymphoma cell expressing integrin α4β7 with IC50 of ≤20 to <100 μmol/L and ≤0.9 μmol/L, resp.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:964135 CAPLUS
DN 138:24543
TI Preparation of benzyloxyphenyloxobutyrates and related compounds for the treatment of metabolic disorders
IN Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA Wellstat Therapeutics Corporation, USA
SO PCT Int. Appl., 242 pp.
CODEN: PIXXD2
DT Patent

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LA   English
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     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2002100341        A2   20021219      WO 2002-US18388  20020612
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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     US 2003149107        A1   20030807      US 2002-167839   20020612
                                             US 2001-297282PP 20010612
     US 2004077896        A1   20040422      US 2003-684644   20031014
                                             US 2001-297282PP 20010612
                                             US 2002-167839 A320020612
OS   MARPAT 138:24543
IT   478162-62-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzyloxyphenyloxobutyrates and related compds. for
        treatment of metabolic disorders)
RN   478162-62-8  CAPLUS
CN   Benzenebutanoic acid, 2,6-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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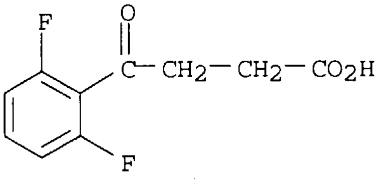

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IT   478163-14-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of benzyloxyphenyloxobutyrates and related compds. for
        treatment of metabolic disorders)
RN   478163-14-3  CAPLUS
CN   Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, 1,1-dimethylethyl ester
     (9CI)  (CA INDEX NAME)
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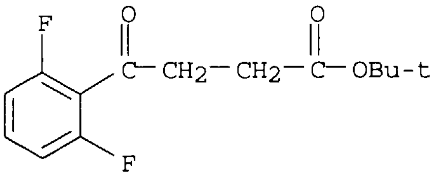

alkoxy, lower alkenyloxy, NO2, amidino, cyano, etc.; provided that when both Y and Z = substituted Ph, at least one of them has a OH group] are prepared These compds. I inhibit strongly tyrosine kinase, suppress tumor cell growth, and thereby are useful as antitumor agents. Thus, 201.5 mg 1,4-di(3,4-dimethoxyphenyl)-1,3-butanedione and 27 μL hydrazine hydrate were dissolved in EtOH and refluxed for 1 h to give 213 mg a pyrazole derivative (II; R = Me), which (19.8 mg) was treated with BBr3 in CH2C12 at -78° for 12 h to give 12.4 mg II (R = H). A furanone derivative [(E)-III; R5 = allyl] and a reference compound (E)-III (R5 = OH) showed IC50 of <18.7 and 72.1 μM, resp., for the inhibition of tyrosine kinase which was measured by determining tyrosine autophosphorylation in the epidermal growth factor receptor induced by human epidermal growth factor in human epidermoid carcinoma A431 cells. A total of 151 I were prepared

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L5   ANSWER 58 OF 69  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1995:812770  CAPLUS
DN   123:228895
TI   Preparation of 2-amino-4-phenyl-4-oxobutyric acid derivatives with
     kynureninase and/or kynurenine-3-hydroxylase inhibiting activity.
IN   Varasi, Mario; Giordani, Antonio; Speciale, Carmela; Cini, Massimo;
     Bianchetti, Alberto
PA   Pharmacia S.p.A., Italy
SO   PCT Int. Appl., 79 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
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PI   WO 9503271        A1   19950202      WO 1994-EP2280    19940712
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         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
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OS   MARPAT 123:228895

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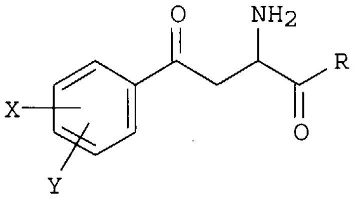

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AB   Title compds. (I; X, Y = H, halo, CF3, OH, alkyl, PhCH2, aryl, OR', SR', SOR', SO2R'; R' = alkyl, PhCH2; R = OH, amino, hydroxylamino, OR', NHR', NR'R', NHOR'), were prepared for prevention and/or treatment of neurodegenerative diseases. Thus, di-Et α-formamidomalonate was stirred 45 min in EtOH containing NaOEt at 45-50°; α-bromo-2'-methoxyacetophenone in EtOH was added and the mixture was stirred 24 h at room temperature to give Et 4-(2'-methoxyphenyl)-4-oxo-2-formylamino-2-ethoxycarbonylbutyrate. This was refluxed in a mixture of HOAc/aqueous HCl to give 2-amino-4-(2'-methoxyphenyl)-4-oxobutyric acid (II) hydrochloride. II inhibited kynureninase by 96% at 100 μM; capsules and injections containing II were prepared

L5   ANSWER 59 OF 69 CAPLUS COPYRIGHT 2004 ACS on STN
AN   1995:713949 CAPLUS
DN   **123:112724**
TI   Preparation of dihydrokynurenine and related compounds as inhibitors of kynureninase.
IN   Phillips, Robert S.; Cyr, Lakshmi V.
PA   University of Georgia Research Foundation, Inc., USA
SO   PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 4

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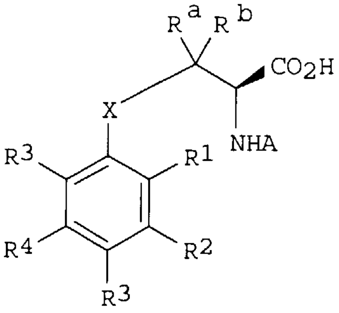

I

AB Title compds. [I; X = CO, CH(OH); Ra, Rb = H, halo, halovinyl, alkyl, haloalkyl; A = H, Ac; R1 = H, NH2, NR6R7, NO2, halo, CF3, alkyl; R6, R7 = H, CHO, alkyl; only 1 of R6, R7 can = CHO; R2 = OH, H, halo, CF3, alkyl; R3, R4, R5 = H, halo, CF3, NO2, NH2, alkyl; with the proviso that when X = CH(OH), neither Ra nor Rb can = CF3], were prepared Thus, L-kynurenine was reduced with NaBH4 in H2O to give dihydrokynurenine (α,2-diamino-γ-hydroxybenzenebutanoic acid) as a separable mixture of (αS,γS)- and (αS,γR)-isomers. The (αS,γS)-isomer inhibited rat liver kynureninase with Ki = 690 μM.

10684730

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L7    ANSWER 20 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    1997:780649  CAPLUS
DN    128:48214
TI    Preparation of 3,5-diphenyl-2(5H)-furanone derivatives as nonpeptide
      endothelin I antagonists
IN    Berryman, Kent Alan; Doherty, Annette Marian; Edmunds, Jeremy John; Patt,
      William Chester; Plummer, Mark Stephen; Repine, Joseph Thomas
PA    Warner-Lambert Co., USA
SO    U.S., 120 pp., Cont.-in-part of U.S. Ser. No. 278,882, abandoned.
      CODEN: USXXAM
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OS MARPAT 128:48214

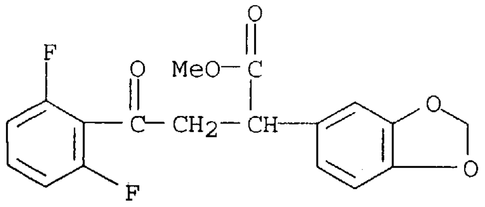
IT **169803-96-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diphenylfuranone derivs. as nonpeptide endothelin I antagonists for disease treatment)

RN 169803-96-7 CAPLUS

CN 1,3-Benzodioxole-5-acetic acid, α-[2-(2,6-difluorophenyl)-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)



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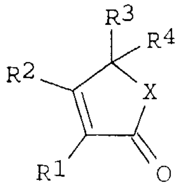

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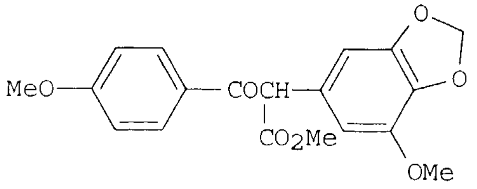

II

AB Novel nonpeptide antagonists of endothelin I represented by formula [I; R1 = (un)substituted C3-12 cycloalkyl, Ph substituted with 1-5 substituents, naphthyl or heteroaryl optionally substituted with 1-5 substituents; R2 = C1-12 linear or branched alkyl, C3-12 linear or branched cycloalkyl, aryl optionally substituted with 1-5 substituents, heteroaryl optionally substituted with 1-3 substituents; R3 = (un)substituted C1-12 linear or branched alkyl, (un)substituted C3-12 cycloalkyl, aryl optionally substituted with 1-5 substituents, heteroaryl optionally substituted with 1-3 substituents; R4 = OH, OR5, (CH2)nOR5; wherein R5 = (un)substituted C1-7 alkyl; X = O, S] or tautomeric open chain keto-acids forms thereof or pharmaceutically acceptable salt thereof are prepared Also described are pharmaceutical compns. of the above compds., which are useful in treating elevated levels of endothelin, acute and chronic renal failure, hypertension, myocardial infarction, myocardial ischemia, cerebral vasospasm, cerebral ischemia, cerebral infarction, cirrhosis, septic shock, congestive heart failure, endotoxic shock, subarachnoid hemorrhage, arrhythmia, asthma, preeclampsia, atherosclerotic disorders including Raynaud's disease and restenosis, angina, cancer, pulmonary hypertension, ischemic disease, gastric mucosal damage, hemorrhagic shock, ischemic bowel disease, stroke, benign prostatic hyperplasia (BPH), and diabetes. Thus, Me 2-benzoyl-2-phenylacetate derivative (II) and 3,4,5-trimethoxybenzladehyde were refluxed in the presence of NaOMe in MeOH for 18 h and the solution was treated with AcOH and refluxed an addnl. 72 h, followed by saponification of the product with 1N aqueous NaOH and acidification to give 28% I (X = O, R1 = Q, R2 = 3,4,5-trimethoxyphenyl, R3 = 4-methoxyphenyl, R4 = OH). The latter compound in vitro showed an antagonism of endothelin I-stimulated vasoconstriction in the rabbit femoral artery and sarafotoxin 6c-stimulated vasoconstriction in the rabbit pulmonary artery with pA2 values of 0.00025 and 0.34, resp.

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FILE 'MARPAT' ENTERED AT 17:13:44 ON 27 APR 2004
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FILE CONTENT: 1988-PRESENT (VOL 140 ISS 17)(20040423/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US    6709645 23 MAR 2004
DE   10335606 11 MAR 2004
EP    1403278 31 MAR 2004
JP 2004099560 02 APR 2004
WO 2004024934 25 MAR 2004

Structure search limits have been raised.  See HELP SLIMIT for the new,
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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)
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    This file contains CAS Registry Numbers for easy and accurate
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    now searchable from 1907-1966.  TIFF images of CA abstracts
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    This file supports REG1stRY for direct browsing and searching of
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Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



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L5             1 L4

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SEARCH PROFILE NOT SUPPORTED FOR AUTOMATED SEARCH AND CROSSOVER
The search profile contains L-numbers or saved item names that include
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FILE COVERS 1907 - 27 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 26 Apr 2004  (20040426/ED)

  This file contains CAS Registry Numbers for easy and accurate
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DN   138:14019
TI   Preparation of 7-(1-pyrrolidinyl)-3-quinolonecarboxylic acids and
     naphthyridone-3-carboxylic acid analogs as antibacterial agents and feed
     additives
IN   Petersen, Uwe; Schenke, Thomas; Krebs, Andreas; Grohe, Klaus; Schriewer,
     Michael; Haller, Ingo; Metzger, Karl G.; Endermann, Rainer; Zeiler,
     Hans-Joachim
PA   Bayer Aktiengesellschaft, Germany
SO   U.S., 52 pp., Division of U.S. 5,416,096.
     CODEN: USXXAM
DT   Patent
LA   English
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US 1991-737631 A3 19910730

OS MARPAT 138:14019
IT **477351-00-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolidinyl quinolonecarboxylate and naphthyridonecarboxylate antibacterial agents by coupling haloheteroarylcarboxylates with pyrrolidines)
RN 477351-00-1 CAPLUS
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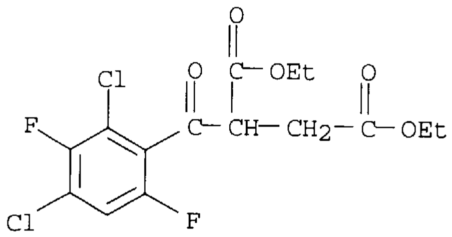

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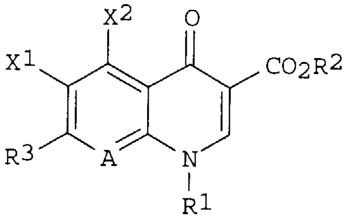

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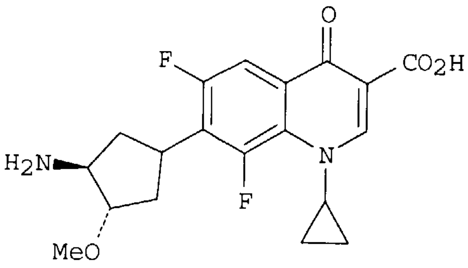

II

AB The title compds. I [wherein R1 = (cyclo)alkyl, alkenyl, 2-hydroxyethyl, 2-fluoroethyl, MeO, NH2, MeNH, EtNH, Me2N, or (fluoro)phenyl; R2 = H, alkyl, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = (un)substituted (fused) pyrrolidinyl; R4 = H, alkyl, aryl, or acyl; X1 = halo; X2 = H, NH2, (di)alkylamino, OH, alkoxy, SH, alkylthio, arylthio, or halo; A = N or CR8; R8 = H, halo, Me, CN, NO2, OH, or OMe; or R1R8 = OCH2CH(Me), SCH2CH(Me), or CH2CH2CH(Me); and their pharmaceutically usable hydrates, acid addition salts, alkali metal, alkaline earth metal, silver, and guanidinium salts thereof] were prepared for use as bactericides and feed additives. Thus, (trans)-3-tert-butoxycarbonylamino-4-methoxypyrrolidine (preparation given) was coupled with 1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid in the presence of 1,4-diazabicyclo[2.2.2]octane in MeCN and DMF. The resulting pyrrolidinylquinolone was converted to the HCl salt (II•HCl) in 70% yield over 2 steps. The latter exhibited antibacterial activity against E. coli, P. mirabilis, P. vulgaris, M. morganii, P. stuartei, S. aureus, and E. faecalis with MIC values (mg/l) of ≤0.015, 1, ≤0.015, ≤0.015, 1, 0.06, and 0.125,

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      resp.
RE.CNT  22      THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11   ANSWER 2 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    2002:960712  CAPLUS
DN    138:14018
TI    Preparation of 7-(1-pyrrolidinyl)-3-quinolonecarboxylic acids and
      naphthyridone-3-carboxylic acid analogs as antibacterial agents and feed
      additives
IN    Petersen, Uwe; Schenke, Thomas; Krebs, Andreas; Grohe, Klaus; Schriewer,
      Michael; Haller, Ingo; Metzger, Karl G.; Endermann, Rainer; Zeiler,
      Hans-Joachim
PA    Bayer Aktiengesellschaft, Germany
SO    U.S., 54 pp.
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DT    Patent
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OS MARPAT 138:14018

IT **477351-00-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolidinyl quinolonecarboxylate and naphthyridonecarboxylate antibacterial agents by coupling haloheteroarylcarboxylates with pyrrolidines)

RN 477351-00-1 CAPLUS

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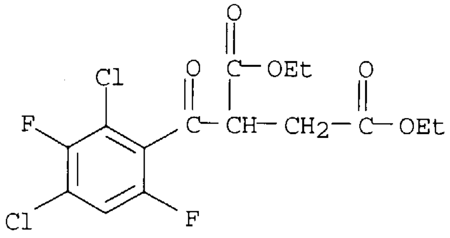

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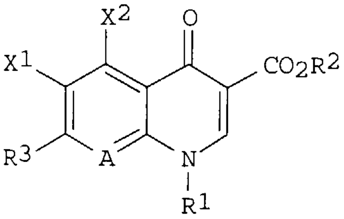

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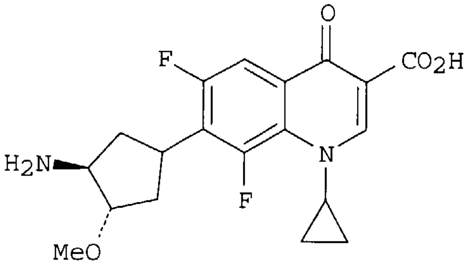

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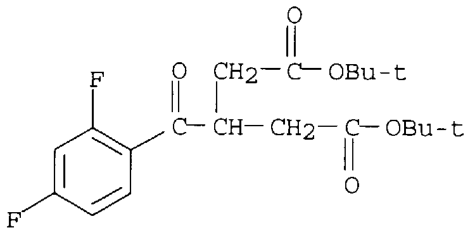
AB The title compds. I [wherein R1 = (cyclo)alkyl, alkenyl, 2-hydroxyethyl, 2-fluoroethyl, MeO, NH2, MeNH, EtNH, Me2N, or (fluoro)phenyl; R2 = H, alkyl, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = (un)substituted (fused) pyrrolidinyl; R4 = H, alkyl, aryl, or acyl; X1 = halo; X2 = H, NH2, (di)alkylamino, OH, alkoxy, SH, alkylthio, arylthio, or halo; A = N or CR8; R8 = H, halo, Me, CN, NO2, OH, or OMe; or R1R8 = OCH2CH(Me), SCH2CH(Me), or CH2CH2CH(Me); and their pharmaceutically usable hydrates, acid addition salts, alkali metal, alkaline earth metal, silver, and guanidinium salts thereof] were prepared for use as bactericides and feed additives. Thus, (trans)-3-tert-butoxycarbonylamino-4-methoxypyrrolidine (preparation given) was coupled with 1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid in the presence of 1,4-diazabicyclo[2.2.2]octane in MeCN and DMF. The resulting pyrrolidinylquinolone was converted to the HCl salt (II•HCl) in 70% yield over 2 steps. The latter exhibited antibacterial activity against E. coli, P. mirabilis, P. vulgaris, M.

morganii, P. stuartei, S. aureus, and E. faecalis with MIC values (mg/l) of ≤0.015, 1, ≤0.015, ≤0.015, 1, 0.06, and 0.125, resp.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:59018 CAPLUS
DN 136:262969
TI Synthesis of Mono- and Difluoronaphthoic Acids
AU Tagat, Jayaram R.; McCombie, Stuart W.; Nazareno, Dennis V.; Boyle, Craig D.; Kozlowski, Joseph A.; Chackalamannil, Samuel; Josien, Hubert; Wang, Yuguang; Zhou, Guowei
CS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA
SO Journal of Organic Chemistry (2002), 67(4), 1171-1177
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:262969
IT **405196-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(formation of dialkyl keto-ester in preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
RN 405196-58-9 CAPLUS
CN Pentanedioic acid, 3-(2,4-difluorobenzoyl)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



IT **405196-57-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
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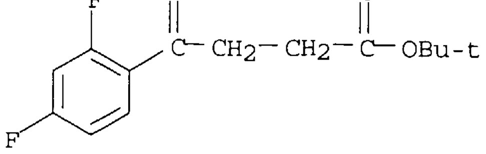
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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AB   Aryl carboxamides are useful structural units found in several biol.
     active compds.  Unlike their benzoic acid counterparts, fluorinated
     versions of naphthoic acids are relatively unknown.  In connection with a
     recent project, we needed viable syntheses of several mono- and
     difluorinated naphthoic acids.  Herein we describe the synthesis of 5-,
     6-, 7-, and 8-fluoro-1-naphthalenecarboxylic acids and 5,7-, 5,8-, 6,7-,
     and 4,5-difluoro-1-naphthalenecarboxylic acids.  The
     5-fluoronaphthoic acid was obtained from the corresponding 5-bromo compound
     via electrophilic fluorination of the lithio-intermediate.  The remaining
     6-fluoro-, 7-fluoro-, 8-fluoro-, 5,7-difluoro-, 5,8-
     difluoro- and 6,7-difluoronaphthoic acids were prepared by a new,
     general route involving conversion of com. fluorinated phenylacetic acids
     to 2-(fluoroaryl)glutaric acids with differential ester groups; selective
     hydrolysis to a mono acid, intramol. Friedel-Crafts cyclization, and
     aromatization furnished the target structures.  An alternative process to
     assemble a naphthalene skeleton is also presented for the 5,7-
     difluoro- and 5,8-difluoronaphthoic acids.  Finally, 4,5-
     difluoro-1-naphthalenecarboxylic acid was prepared expeditiously
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RE.CNT  16     THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L11  ANSWER 4 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1996:524249  CAPLUS
DN   125:195657
TI   Benzocycloalkylazolethione derivatives useful as dopamine
     β-hydroxylase inhibitors.
IN   Martinez, Gregory R.; Gooding, Owen W.; Repke, David B.; Teitelbaum,
     Philip J.; Walker, Keith A. M.; Whiting, Roger L.
PA   USA
SO   U.S., 55 pp., Cont.-in-part of U.S. Ser. No. 233,835, abandoned.
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IT **170151-15-2P**
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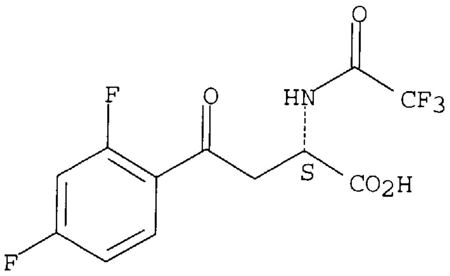
(intermediate; preparation of benzocycloalkylazolethione derivs. as dopamine β-hydroxylase inhibitors)
RN 170151-15-2 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-[(trifluoroacetyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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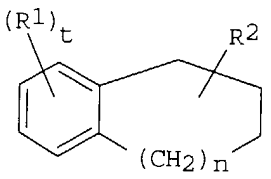

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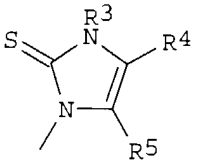

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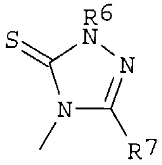

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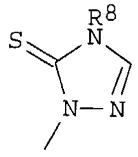

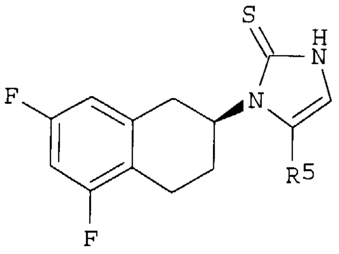

II

AB The invention relates to novel benzocycloalkylazolethiones I [n = 0-2; t = 0-3; R1 = halo, OH, alkoxy; R2 = imidazole group Q1 or triazole group Q2 or Q3; R3 = H, (un)substituted NH2, (CH2)qR9, etc.; q = 0-4; R4 = H, , alkyl, CO2H, carbamoyl, etc.; R5 = H, (un)substituted NH2, etc.; R6 = H, CH2CH2CO2H, CH2CH2CONH2, etc.; R7 = H, (un)substituted CH2NH2; R8 = groups given for R6, or (un)substituted NH2; R9 = CO2H or derivs., (un)substituted aryl or heteroaryl, etc.] and related compds. The compds. are are dopamine β-hydroxylase inhibitors, and are thus peripheral vasodilators useful in the treatment of hypertension and congestive heart failure (no data). For example, (S)-5,7-**difluoro** -1,2,3,4-tetrahydronaphthalen-2-ylamine-HCl [preparation given] reacted with

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     formaldehyde-Na bisulfite complex and KCN to give the N-(cyanomethyl)
     derivative, which underwent N-formylation with HCO2Bu, α-condensation
     with HCO2Et, and cyclization with KSCN, to give title compound II [R5 =
     cyano]. This was reduced with LiAlH4 in THF to give II [R5 = CH2NH2].

L11  ANSWER 5 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1995:998191  CAPLUS
DN   124:176116
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     β-hydroxylase inhibitors.
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     Keith A. M.; Gooding, Owen W.; Whiting, Roger L.; Bansal, Rekha P.;
     Muehldorf, Alexander V.; O'yang, Counde
PA   Syntex (U.S.A.) Inc., USA
SO   PCT Int. Appl., 146 pp.
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        (preparation of benzocycloalkylazolethione derivs. as dopamine
        β-hydroxylase inhibitors)
RN   170151-15-2  CAPLUS
CN   Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-
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Absolute stereochemistry.  Rotation (+).
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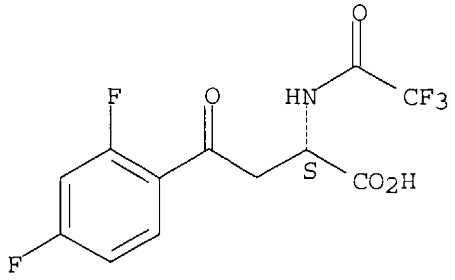

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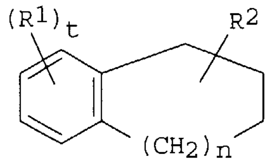

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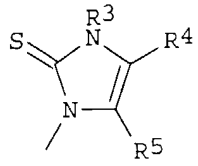

AB Title compds. [I; n = 0-2; t = 0-3; q = 0-4; R1 = halo, OH, alkyloxy; R2 = Q1, etc.; R3 = H, amino, (CH2)qR9; R4 = H; R5 = H, amino, acylamino; R9 = CO2H, alkoxycarbonyl, carbamoyl, (substituted) aryl, heteroaryl; with provisos] were prepared as dopamine β-hydroxylase inhibitors. Thus, (S)-5-aminomethyl-1-(5,7-**difluoro**-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione hydrochloride (preparation given) at 10 mg/kg in rats reduced mean arterial blood pressure by 53 mm Hg.

L11 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
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TI Process for making 1-benzocycloalkyl-1,3-dihydroimidazole-2-thione derivatives via cyclization of benzocycloalkylamines with thiocyanic acid and dihydroxyacetone
IN Bansal, Rekha P.; Gooding, Owen W.; Muehldorf, Alexander V.; O-Yang, Counde
PA Syntex (U.S.A.) Inc., USA
SO U.S., 16 pp.
CODEN: USXXAM
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FAN.CNT 3

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IT **170151-15-2P**

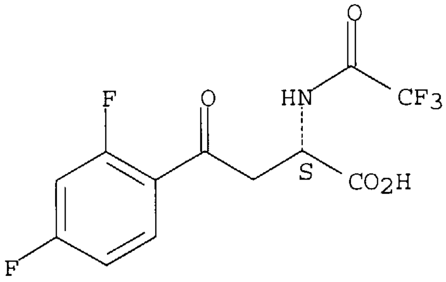
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 1-benzocycloalkyl-1,3-dihydroimidazole-2-thione derivs. via cyclization of benzocycloalkylamines with thiocyanic acid and dihydroxyacetone)

RN 170151-15-2 CAPLUS

CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-[(trifluoroacetyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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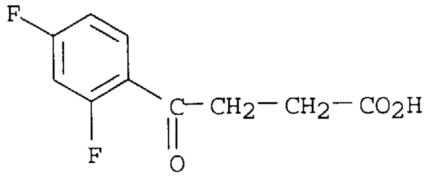
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to a process for preparing an acid addition salt of title compds. I in which: n is 0, 1 or 2; m is 0, 1, 2 or 3; R1 is independently halo, hydroxy or (C1-4)alkyloxy; or the free base, an individual stereoisomer, or a mixture of stereoisomers thereof, which process comprises (A) reacting a benzocycloalkylamine II with thiocyanic acid and dihydroxyacetone to give a corresponding 5-hydroxymethyl-1-benzocycloalkyl-1,3-dihydroimidazole-2-thione III and then (B) reacting III with a compound of the formula H2NCOR2 or an ammonium salt of the formula NH4+-OC(O)R2 [in which R2 is hydrogen, (C1-4)alkyl or trifluoro(C1-4)alkyl] to give IV; and (C) hydrolyzing IV with acid; and (D) optionally reacting the acid addition salt of I with an inorg. or organic base to give the corresponding free base form; and (E) optionally reacting the free base form of I with a pharmaceutically acceptable acid to give the corresponding acid addition salt; and (F) optionally separating a mixture of stereoisomers of a I to give a single stereoisomer. Thus, e.g., acylation

of 1,3-difluorobenzene with N-(trifluoroacetyl)-L-aspartic anhydride afforded (S)-2-[(trifluoroacetyl)amino]-4-(2,4-difluorophenyl)-4-oxobutanoic acid; hydrogenation of the latter afforded (S)-2-[(trifluoroacetyl)amino]-4-(2,4-difluorophenyl)butanoic acid; cyclization of the latter afforded (S)-5,7-**difluoro** -2-[(trifluoroacetyl)amino]-3,4-dihydro(2H)-naphthalen-1-one which upon hydrogenation and hydrolysis afforded (S)-5,7-**difluoro** -1,2,3,4-tetrahydronaphthalen-2-ylamine hydrochloride [(S)-II with n = 1, m = 2, R1 = 5,7-F2]; the latter was converted to (S)-5-Hydroxymethyl-1-(5,7-**difluoro**-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione (III) with potassium thiocyanate/dihydroxyacetone; reaction of III with formamide afforded (S)-N-[3-(5,7-**difluoro**-1,2,3,4-tetrahydronaphthalen-2-yl)-2-thioxo-2,3-dihydro-1H-imidazol-4-ylmethyl]formamide (IV); treatment of IV with concentrated HCl afforded (S)-5-aminomethyl-1-(5,7-**difluoro** -1,2,3,4-tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione hydrochloride (I.HCl).

L11 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:640906 CAPLUS
DN 119:240906
TI Synthesis and structure-activity relationships of naphthalene-substituted derivatives of the allylamine antimycotic terbinafine
AU Nussbaumer, Peter; Dorfstaetter, Gerhard; Leitner, Ingrid; Mraz, Karin; Vyplel, Hermann; Stuetz, Anton
CS Dep. Dermatol., SANDOZ Forschungsinst., Vienna, A-1235, Austria
SO Journal of Medicinal Chemistry (1993), 36(19), 2810-16
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



AB Derivs. of the allylamine antimycotic terbinafine with varied substitution at the naphthalene ring system have been prepared, and their antifungal activity has been evaluated. In general, the potency is strongly dependent on the bulkiness of the substituent,. Only hydrogen or in some cases fluorine are tolerated as substituents at positions 2-4 and 6-8 of the naphthalene moiety, whereas 5-substituents may be larger in size (F, Cl, Br, Me). Derivs. with fluorine at positions 3, 5, and 7 or chlorine at position 5 showed enhanced activity against yeasts relative to terbinafine. This increase in sensitivity could be intensified by simultaneous introduction of two fluoro substituents at positions 5 and 7. One compound prepared demonstrated an 8- to 16-fold improved potency against Aspergillus fumigatus, Candida albicans, and Candida parapsilosis.

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L11  ANSWER 8 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1989:423238  CAPLUS
DN   111:23238
TI   New allylamine derivatives, their preparation, and their use as
     antimycotics
IN   Nussbaumer, Peter; Stuetz, Anton; Vyplel, Hermann; Enzersdorf, Maria
PA   Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO   Ger. Offen., 10 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
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PI   DE 3720317         A1   19881229      DE 1987-3720317   19870619
                                           DE 1987-3720317   19870619
OS   CASREACT 111:23238; MARPAT 111:23238
IT   110931-77-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, in synthesis of allylnaphthylmethylamine
        fungicide)
RN   110931-77-6  CAPLUS
CN   Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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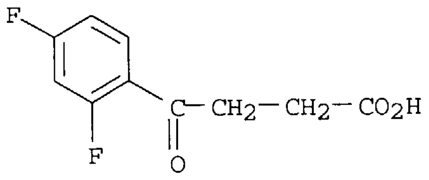

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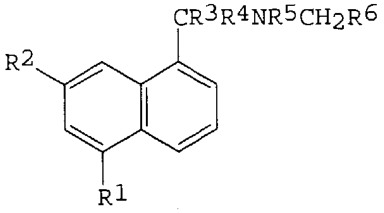
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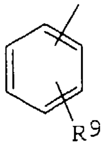
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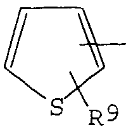
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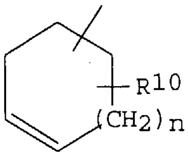
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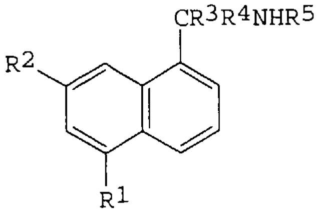
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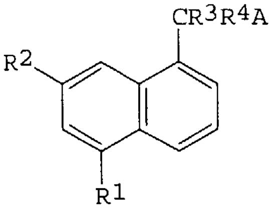
III

AB Naphthalenes I [R1,R2 = H, F; R1 = R2 ≠ H; R3, R4, R5 = H, alkyl;
R4, R5 = (CH)2)m ; R5 = CH:CHC.tplbond.CR7, CH:CHCH:CHR7,
CH2C.tplbond.CR78 CH:CHR8; R7 = alkyl, cycloalkyl, trialkylsilyl,
dialkylphenylsilyl, phenylalkyl, or alkenyl (un)substituted by alkyl,
alkoxy, Ph, or halo; R8 = Q, Q1, Q2; R9 = halo, CF3, alkyl, alkyl, H; R10
= H, alkyl; m = 3,4,5; n = 0-2] and their acid salts, useful as medicinal
and agrochem. fungicides, were prepared:a) by reaction of amine II with
ACH2R6 (A = cleavable group), or b) by reaction of III with R5NH = CH2R6
and optional conversion of the products into acid addition salts.
Me3CC.tplbond.CCH:CHCH2Br [(E):(Z) = 3:1] in DMF was added dropwise to
(5,7-**difluoro**-1-naphthylmethyl)methylamine (prepared in 7 steps
from 1,3-F2C6H4, AlCl3, and succinic anhydride) and K2CO3 in DMF and the
mixture kept 4 h at room temperature to give (E)- and (Z)-I (R1 = R2 = F, R3 =
R4
= H, R5 = Me, R6 = CH:CHC.tplbond.CCMe3) (V). The curative dose for V in
treating guinea pigs infected with Trichophyton mentagrophytes was 9
+ 6 mg/kg in miglyol vs. 9 + 70 mg/kg for griseofulvin.

L11 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:617260 CAPLUS
DN 107:217260
TI Preparation of arylmethylamines as antimycotics and agrochemical
fungicides
IN Stuetz, Anton; Nussbaumer, Peter
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 34 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

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US 4939148	A	19900703	US 1987-8198	19870129
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CA 1329619	A1	19940517	CA 1987-528508	19870129
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			DE 1986-3609123	19860319
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FR 2643224	A1	19900824	FR 1990-3701	19900320
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			DE 1986-3617637	19860526
US 5112851	A	19920512	US 1990-520577	19900508
			DE 1986-3602579	19860129
			DE 1986-3609123	19860319
			DE 1986-3617635	19860526
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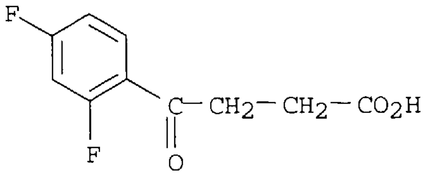
			US 1987-8198	19870129

IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



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GI   For diagram(s), see printed CA Issue.
AB   R1R2CHNR3CR4R5R6 [I; R1 = Q-Q5; R2 = H, alkyl; R1R2 = Q6; R2R3 = (CH2)m;
     R7, R8 = H, halo, CF3, alkyl, alkoxy; R9 = H, halo, alkyl, alkoxy; R10,
     R11 = H, alkyl, halo, CF3, alkoxy, alkylthio; X = O, S, NH, alkylimino,
     CH2, OCH2; p = 1-3; s = 3-5; n = 3-6; m = 1-8; in Q3, CH2 may be replaced
     by O or S; R4, R5 = H, alkyl; R3 = H, cycloalkyl, (halo)alkyl; R6 =
     Q7-Q10; w = 2-6; Z = O, S, NR3; R12 = aliphatic, cycloalkyl, alkoxy,
     alkoxycarbonyl, alkylthio, Ph, etc.], were prepared as antimycotics and
     agrochem. fungicides (no data).  A mixture of 4-Me3CC6H4CH2NHMe, K2CO3, and
     DMF was treated with 1-(bromomethyl)-5,7-difluoronaphthalene and stirred
     overnight to give N-benzyl-1-naphthalenemethylamine II.


=> d l15 fbib hitstr abs total

L15  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:960716  CAPLUS
DN   138:14019
TI   Preparation of 7-(1-pyrrolidinyl)-3-quinolonecarboxylic acids and
     naphthyridone-3-carboxylic acid analogs as antibacterial agents and feed
     additives
IN   Petersen, Uwe; Schenke, Thomas; Krebs, Andreas; Grohe, Klaus; Schriewer,
     Michael; Haller, Ingo; Metzger, Karl G.; Endermann, Rainer; Zeiler,
     Hans-Joachim
PA   Bayer Aktiengesellschaft, Germany
SO   U.S., 52 pp., Division of U.S. 5,416,096.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   US 5607942         A    19970304       US 1995-406448   19950320
                                            DE 1988-3824072A 19880715
                                            DE 1989-3906365A 19890301
                                            US 1989-375434 A319890630
                                            US 1990-580906 A319900910
                                            US 1991-737631 A319910730
     DE 3906365         A1   19900118       DE 1989-3906365  19890301
                                            DE 1988-3824072A119880715
     US 4990517         A    19910205       US 1989-375434   19890630
                                            DE 1988-3824072A 19880715
                                            DE 1989-3906365A 19890301
     US 5059597         A    19911022       US 1990-580906   19900910
                                            DE 1988-3824072A 19880715
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                                            US 1989-375434 A319890630
     US 5416096         A    19950516       US 1991-737631   19910730
                                            DE 1988-3824072A 19880715
                                            DE 1989-3906365A 19890301
```
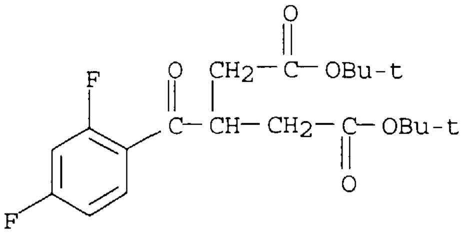
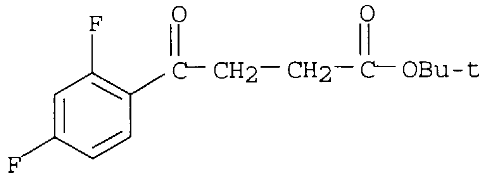

AB The title compds. I [wherein R1 = (cyclo)alkyl, alkenyl, 2-hydroxyethyl, 2-fluoroethyl, MeO, NH2, MeNH, EtNH, Me2N, or (fluoro)phenyl; R2 = H, alkyl, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = (un)substituted (fused) pyrrolidinyl; R4 = H, alkyl, aryl, or acyl; X1 = halo; X2 = H, NH2, (di)alkylamino, OH, alkoxy, SH, alkylthio, arylthio, or halo; A = N or CR8; R8 = H, halo, Me, CN, NO2, OH, or OMe; or R1R8 = OCH2CH(Me), SCH2CH(Me), or CH2CH2CH(Me); and their pharmaceutically usable hydrates, acid addition salts, alkali metal, alkaline earth metal, silver, and guanidinium salts thereof] were prepared for use as bactericides and feed additives. Thus, (trans)-3-tert-butoxycarbonylamino-4-methoxypyrrolidine (preparation given) was coupled with 1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid in the presence of 1,4-diazabicyclo[2.2.2]octane in MeCN and DMF. The resulting pyrrolidinylquinolone was converted to the HCl salt (II•HCl) in 70% yield over 2 steps. The latter exhibited antibacterial activity against E. coli, P. mirabilis, P. vulgaris, M. morganii, P. stuartei, S. aureus, and E. faecalis with MIC values (mg/l) of ≤0.015, 1, ≤0.015, ≤0.015, 1, 0.06, and 0.125, resp.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:59018 CAPLUS
DN 136:262969
TI Synthesis of Mono- and Difluoronaphthoic Acids
AU Tagat, Jayaram R.; McCombie, Stuart W.; Nazareno, Dennis V.; Boyle, Craig D.; Kozlowski, Joseph A.; Chackalamannil, Samuel; Josien, Hubert; Wang, Yuguang; Zhou, Guowei
CS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA
SO Journal of Organic Chemistry (2002), 67(4), 1171-1177
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:262969
IT **405196-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(formation of dialkyl keto-ester in preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
RN 405196-58-9 CAPLUS
CN Pentanedioic acid, 3-(2,4-difluorobenzoyl)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



IT **405196-57-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
RN 405196-57-8 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

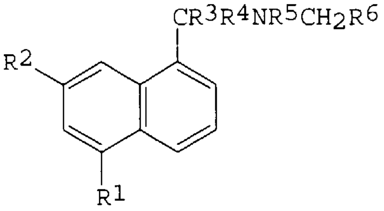


AB Aryl carboxamides are useful structural units found in several biol. active compds. Unlike their benzoic acid counterparts, fluorinated versions of naphthoic acids are relatively unknown. In connection with a recent project, we needed viable syntheses of several mono- and difluorinated naphthoic acids. Herein we describe the synthesis of 5-, 6-, 7-, and 8-fluoro-1-naphthalenecarboxylic acids and 5,7-, 5,8-, 6,7-, and 4,5-**difluoro**-1-naphthalenecarboxylic acids. The 5-fluoronaphthoic acid was obtained from the corresponding 5-bromo compound via electrophilic fluorination of the lithio-intermediate. The remaining 6-fluoro-, 7-fluoro-, 8-fluoro-, 5,7-**difluoro**-, 5,8-**difluoro**- and 6,7-difluoronaphthoic acids were prepared by a new, general route involving conversion of com. fluorinated phenylacetic acids to 2-(fluoroaryl)glutaric acids with differential ester groups; selective hydrolysis to a mono acid, intramol. Friedel-Crafts cyclization, and aromatization furnished the target structures. An alternative process to assemble a naphthalene skeleton is also presented for the 5,7-**difluoro**- and 5,8-difluoronaphthoic acids. Finally, 4,5-**difluoro**-1-naphthalenecarboxylic acid was prepared expeditiously from 1,8-diaminonaphthalene by adapting classical reactions.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:524249 CAPLUS
DN 125:195657
TI Benzocycloalkylazolethione derivatives useful as dopamine β-hydroxylase inhibitors.
IN Martinez, Gregory R.; Gooding, Owen W.; Repke, David B.; Teitelbaum, Philip J.; Walker, Keith A. M.; Whiting, Roger L.
PA USA
SO U.S., 55 pp., Cont.-in-part of U.S. Ser. No. 233,835, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5538988	A	19960723	US 1995-403209	19950317
				US 1994-233835	B219940426

GI



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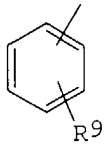

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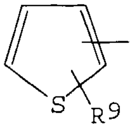

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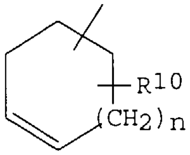

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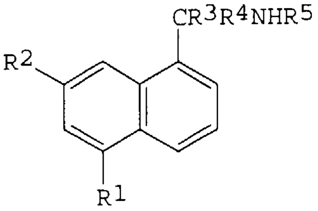

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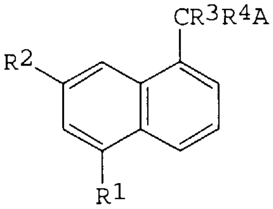

III

AB Naphthalenes I [R1,R2 = H, F; R1 = R2 ≠ H; R3, R4, R5 = H, alkyl; R4, R5 = (CH)2)m ; R5 = CH:CHC.tplbond.CR7, CH:CHCH:CHR7, CH2C.tplbond.CR78 CH:CHR8; R7 = alkyl, cycloalkyl, trialkylsilyl, dialkylphenylsilyl, phenylalkyl, or alkenyl (un)substituted by alkyl, alkoxy, Ph, or halo; R8 = Q, Q1, Q2; R9 = halo, CF3, alkyl, alkyl, H; R10 = H, alkyl; m = 3,4,5; n = 0-2] and their acid salts, useful as medicinal and agrochem. fungicides, were prepared:a) by reaction of amine II with ACH2R6 (A = cleavable group), or b) by reaction of III with R5NH = CH2R6 and optional conversion of the products into acid addition salts. Me3CC.tplbond.CCH:CHCH2Br [(E):(Z) = 3:1] in DMF was added dropwise to (5,7-**difluoro**-1-naphthylmethyl)methylamine (prepared in 7 steps from 1,3-F2C6H4, AlCl3, and succinic anhydride) and K2CO3 in DMF and the mixture kept 4 h at room temperature to give (E)- and (Z)-I (R1 = R2 = F, R3 =
R4
= H, R5 = Me, R6 = CH:CHC.tplbond.CCMe3) (V). The curative dose for V in treating guinea pigs infected with Trichophyton mentagrophytes was 9 + 6 mg/kg in miglyol vs. 9 + 70 mg/kg for griseofulvin.

L15 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:617260 CAPLUS
DN 107:217260
TI Preparation of arylmethylamines as antimycotics and agrochemical fungicides
IN Stuetz, Anton; Nussbaumer, Peter
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 34 pp.

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     CODEN: GWXXBX
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LA   German
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     GB 2185980          B2   19900815
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     FR 2597475          A1   19871023        FR 1987-973       19870126
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US 5112851	A	19920512	US 1990-520577	19900508
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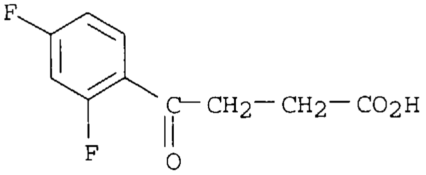
			US 1987-8198	19870129

IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



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GI   For diagram(s), see printed CA Issue.
AB   R1R2CHNR3CR4R5R6 [I; R1 = Q-Q5; R2 = H, alkyl; R1R2 = Q6; R2R3 = (CH2)m;
     R7, R8 = H, halo, CF3, alkyl, alkoxy; R9 = H, halo, alkyl, alkoxy; R10,
     R11 = H, alkyl, halo, CF3, alkoxy, alkylthio; X = O, S, NH, alkylimino,
     CH2, OCH2; p = 1-3; s = 3-5; n = 3-6; m = 1-8; in Q3, CH2 may be replaced
     by O or S; R4, R5 = H, alkyl; R3 = H, cycloalkyl, (halo)alkyl; R6 =
     Q7-Q10; w = 2-6; Z = O, S, NR3; R12 = aliphatic, cycloalkyl, alkoxy,
     alkoxycarbonyl, alkylthio, Ph, etc.], were prepared as antimycotics and
     agrochem. fungicides (no data).  A mixture of 4-Me3CC6H4CH2NHMe, K2CO3, and
     DMF was treated with 1-(bromomethyl)-5,7-difluoronaphthalene and stirred
     overnight to give N-benzyl-1-naphthalenemethylamine II.


=> d his

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                  S L1

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L6              1 S L2

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L8             78 S L3
L9             40 S L6
L10             0 S L7 AND 2,6-DIFLUORO
L11             9 S L7 AND DIFLUORO
L12             0 S L8 AND DISLUORO
L13             0 S L8 AND DIFLUORO
L14             0 S L8 AND 2,6-DIFLUORO
L15             9 S L9 AND DIFLUORO

=> d l8 fbib hitstr abs total

L8   ANSWER 1 OF 78  CAPLUS  COPYRIGHT 2004 ACS on STN
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     alkoxy, lower alkenyloxy, NO2, amidino, cyano, etc.; provided that when
     both Y and Z = substituted Ph, at least one of them has a OH group] are
     prepared These compds. I inhibit strongly tyrosine kinase, suppress tumor
     cell growth, and thereby are useful as antitumor agents.  Thus, 201.5 mg
     1,4-di(3,4-dimethoxyphenyl)-1,3-butanedione and 27 μL hydrazine hydrate
     were dissolved in EtOH and refluxed for 1 h to give 213 mg a pyrazole
     derivative (II; R = Me), which (19.8 mg) was treated with BBr3 in CH2Cl2 at
     -78° for 12 h to give 12.4 mg II (R = H).  A furanone derivative
     [(E)-III; R5 = allyl] and a reference compound (E)-III (R5 = OH) showed IC50 of
     <18.7 and 72.1 μM, resp., for the inhibition of tyrosine kinase which
     was measured by determining tyrosine autophosphorylation in the epidermal
growth
     factor receptor induced by human epidermal growth factor in human
     epidermoid carcinoma A431 cells.  A total of 151 I were prepared

L8   ANSWER 68 OF 78  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1995:812770  CAPLUS
DN   123:228895
TI   Preparation of 2-amino-4-phenyl-4-oxobutyric acid derivatives with
     kynureninase and/or kynurenine-3-hydroxylase inhibiting activity.
IN   Varasi, Mario; Giordani, Antonio; Speciale, Carmela; Cini, Massimo;
     Bianchetti, Alberto
PA   Pharmacia S.p.A., Italy
SO   PCT Int. Appl., 79 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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PI   WO 9503271          A1   19950202      WO 1994-EP2280   19940712
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         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                            IT 1993-MI1649 A 19930723
     CA 2144521          AA   19950202      CA 1994-2144521  19940712
                                            IT 1993-MI1649 A 19930723
     AU 9472285          A1   19950220      AU 1994-72285    19940712
     AU 678273           B2   19970522
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     HU 70478            A2   19951030      HU 1995-1146     19940712
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     CN 1112786          A    19951129      CN 1994-190531   19940712
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     JP 08501805         T2   19960227      JP 1994-503289   19940712
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     AT 171935           E    19981015      AT 1994-921642   19940712
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     ES 2123801          T3   19990116      ES 1994-921642   19940712
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     PL 179857         B1    20001130       PL 1994-308142   19940712
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     IL 110365         A1    19980615       IL 1994-110365   19940719
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     ZA 9405425        A     19950301       ZA 1994-5425     19940722
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     US 2001008947     A1    20010719       US 1997-949392   19971014
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OS MARPAT 123:228895
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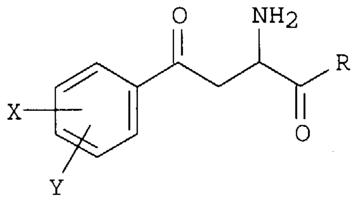

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AB Title compds. (I; X, Y = H, halo, CF3, OH, alkyl, PhCH2, aryl, OR', SR', SOR', SO2R'; R' = alkyl, PhCH2; R = OH, amino, hydroxylamino, OR', NHR', NR'R', NHOR'), were prepared for prevention and/or treatment of neurodegenerative diseases. Thus, di-Et α-formamidomalonate was stirred 45 min in EtOH containing NaOEt at 45-50°; α-bromo-2'-methoxyacetophenone in EtOH was added and the mixture was stirred 24 h at room temperature to give Et 4-(2'-methoxyphenyl)-4-oxo-2-formylamino-2-ethoxycarbonylbutyrate. This was refluxed in a mixture of HOAc/aqueous HCl to give 2-amino-4-(2'-methoxyphenyl)-4-oxobutyric acid (II) hydrochloride. II inhibited kynureninase by 96% at 100 μM; capsules and injections containing II were prepared

L8 ANSWER 69 OF 78 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:713949 CAPLUS
DN **123:112724**
TI Preparation of dihydrokynurenine and related compounds as inhibitors of kynureninase.
IN Phillips, Robert S.; Cyr, Lakshmi V.
PA University of Georgia Research Foundation, Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

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     FILE 'CAOLD' ENTERED AT 17:14:52 ON 27 APR 2004
L5            1 S L4 SSS FULL
L6            1 S L2

     FILE 'CAPLUS' ENTERED AT 17:15:48 ON 27 APR 2004
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L8           78 S L3
L9           40 S L6
L10           0 S L7 AND 2,6-DIFLUORO
L11           9 S L7 AND DIFLUORO
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L15           9 S L9 AND DIFLUORO

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L7   ANSWER 1 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:267316  CAPLUS
DN   140:287370
TI   Preparation of phenyl oxazolidinone derivatives as antimycobacterial
     agents
IN   Arora, Sudershan Kumar; Patil, Vijaykumar Jagdishwar; Nair, Prathap
     Sreedharan; Dixit, Prasad Purushottam; Ajay, Shankar; Sinha, Rakesh Kumar
PA   Lupin Limited, India
SO   PCT Int. Appl., 84 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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PI   WO 2004026848      A1   20040401       WO 2002-IN190    20020920
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             TJ, TM
        RW:  GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                            WO 2002-IN190    20020920
IT   110931-77-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of Ph oxazolidinone derivs. as antimycobacterial agents)
RN   110931-77-6  CAPLUS
CN   Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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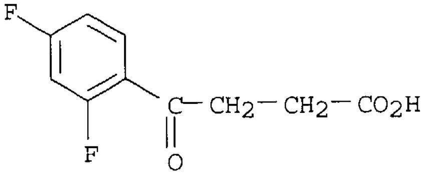

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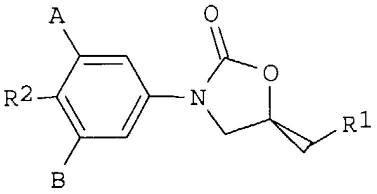

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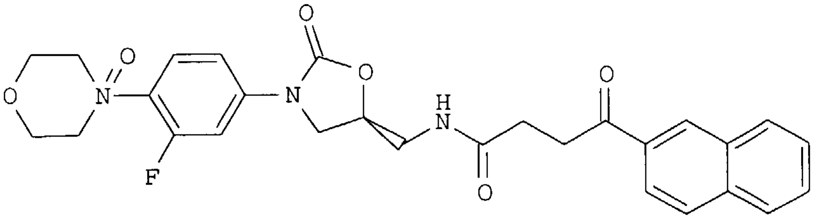

II

AB Oxazolidinones of formula I [A, B = H, F; R1 = NHCOQCYAr; Q = CH2CH2, CH=CH, C.tplbond.C; Y = O, S, (substituted) NH; Ar = (substituted) aryl; R2 = heteroaryl, heterocycloalkyl, (substituted) amino, and N-oxides] are prepared which have potent antimycobacterial properties especially useful in the treatment of acid fast organisms such as Mycobacterium tuberculosis, Mycobacterium avium-intracellular complex, M. fortuitum and M. kansai. The compound and its pharmaceutically acceptable salts thereof act as antibacterial agents. Also disclosed is a method for inhibiting growth of mycobacterial cells a well as a method of treating mycobacterial conditions such as Mycobacterium tuberculosis, drug resistant Mycobacterium tuberculosis, Mycobacterium avium-intracellular complex, M. fortuitum and M. kansai, comprising administering an antimycobacterially effective amount of the said compound and/or pharmaceutically acceptable salts thereof. There is also disclosed a process for the manufacture of the said compound or its pharmaceutically acceptable salts. Thus, II was prepared by coupling the amino fragment with a carboxylic acid. The in vivo activity of II against M. tuberculosis ATCC 27294 infection in Swiss albino mice was comparable to isoniazid.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:3662 CAPLUS
DN 140:77155

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TI   Preparation of water-soluble phenylpyridazine derivatives as IL-β
     inhibitors
IN   Kyotani, Yoshinori; Koshi, Tomoyuki; Shigyo, Hiromichi; Yoshizaki, Hideo;
     Kitamura, Takahiro; Takemura, Shunji; Yasuoka, Kyoko; Totsuka, Junko;
     Sato, Seiichi
PA   Kowa Co., Ltd., Japan
SO   U.S. Pat. Appl. Publ., 82 pp., Cont.-in-part of U.S. Ser. No. 253,523.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.          KIND  DATE            APPLICATION NO.  DATE
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PI   US 2004002497        A1   20040101        US 2003-396726   20030326
                                               US 2001-324569PP 20010926
                                               US 2002-253523 A220020925
     US 2003119838        A1   20030626        US 2002-253523   20020925
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PATENT FAMILY INFORMATION:
FAN  2003:261816
     PATENT NO.          KIND  DATE            APPLICATION NO.  DATE
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PI   WO 2003027077        A1   20030403        WO 2002-JP9863   20020925
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             TJ, TM
        RW:  GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                               US 2001-324569PP 20010926
OS   MARPAT 140:77155
IT   503825-40-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate; preparation of water-soluble phenylpyridazine derivs. as
        IL-β inhibitors)
RN   503825-40-9  CAPLUS
CN   Propanedioic acid, [2-(2,4-difluorophenyl)-2-oxoethyl]hydroxy-, diethyl
     ester (9CI)  (CA INDEX NAME)
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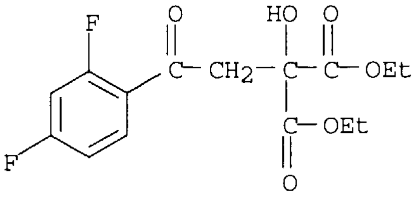

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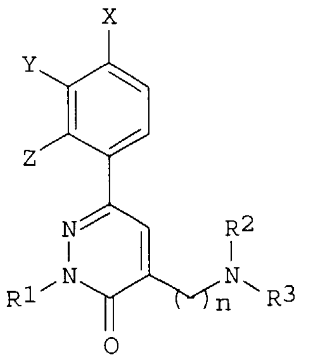
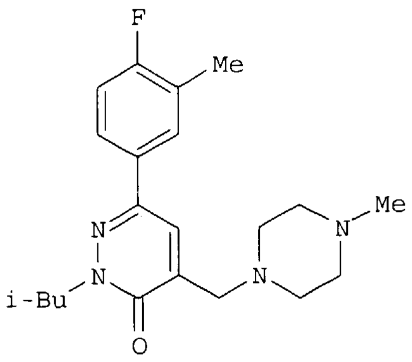


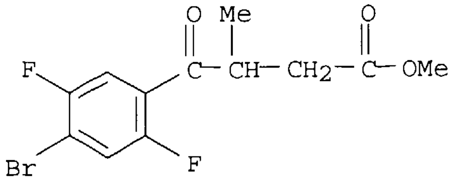
I



II

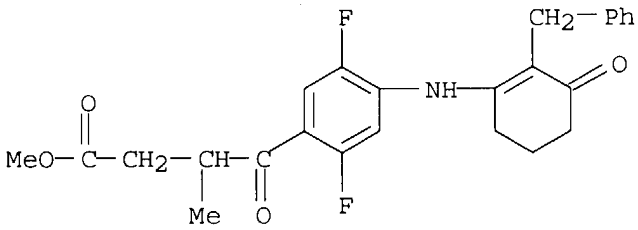
AB The title compds. I [wherein R1 = (un)substituted alkyl or alkenyl; R2 and R3 = H, alkyl, (di)hydroxyalkyl, alkynyl; or NR2R3 = (un)substituted saturated heterocycle; X, Y, and Z = H, halo, (un)substituted alkyl(thio), alkoxy, alkylsulfinyl, alkylsulfonyl, aryl; n = 1-5; with provisos] and their salts are prepared as inhibitors of interleukin (IL) β production For example, the pyridazine II•2HCl was prepared in a multi-step synthesis in a good yield. II•2HCl showed inhibiting activity with IC50 of 0.27 μM against IL-1β production I are highly soluble in water, and have a favorable oral absorbability. Pharmaceutical composition comprising the title compound I is claimed.

L7 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:841823 CAPLUS
DN 140:87057
TI Benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors
AU Edmondson, Scott D.; Mastracchio, Anthony; He, Jiafang; Chung, Christine C.; Forrest, Michael J.; Hofsess, Scott; MacIntyre, Euan; Metzger, Joseph; O'Connor, Naphtali; Patel, Kajal; Tong, Xinchun; Tota, Michael R.; Van der Ploeg, Lex H. T.; Varnerin, Jeff P.; Fisher, Michael H.; Wyvratt, Matthew J.; Weber, Ann E.; Parmee, Emma R.
CS Department of Medicinal Chemistry, Merck & Co., Inc., Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(22), 3983-3987
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
IT **644984-85-0P 644985-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationship of benzyl vinylogous amide substituted aryldihydropyridazinones and aryldimethylpyrazolones as potent and selective PDE3B inhibitors)
RN 644984-85-0 CAPLUS
CN Benzenebutanoic acid, 4-bromo-2,5-difluoro-β-methyl-γ-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 644985-01-3 CAPLUS

CN Benzenebutanoic acid, 2,5-difluoro-β-methyl-γ-oxo-4-[[3-oxo-2-(phenylmethyl)-1-cyclohexen-1-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)



AB Aryldihydropyridazinones and aryldimethylpyrazolones with 2-benzyl vinylogous amide substituents have been identified as potent PDE3B subtype selective inhibitors. One dihydropyridazinone (PDE3B IC50=0.19 nM, 3A IC50=1.3 nM) was selected for in vivo evaluation of lipolysis induction, metabolic rate increase, and cardiovascular effects.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:777799 CAPLUS
DN 139:292257
TI Preparation of pyrazolopyridazines for the inhibition of GSK-3
IN Witherington, Jason; Ward, Robert William
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

```
     PATENT NO.          KIND  DATE           APPLICATION NO.   DATE
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PI   WO 2003080616        A1   20031002       WO 2003-EP3171    20030320
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
            TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
            MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
            CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
            NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
            GW, ML, MR, NE, SN, TD, TG
                                              GB 2002-6723    A 20020321
```

OS MARPAT 139:292257

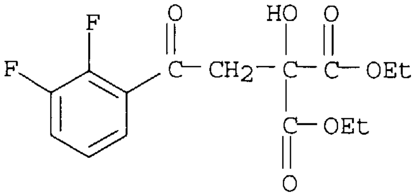
IT **405224-28-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrazolopyridazines as GSK-3 inhibitors)

RN 405224-28-4 CAPLUS

CN Propanedioic acid, [2-(2,3-difluorophenyl)-2-oxoethyl]hydroxy-, diethyl ester (9CI) (CA INDEX NAME)



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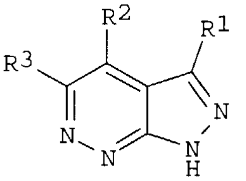

I

AB The title compds. [I; R1 = H, halo, alkyl, hydroxyalkyl, (un)substituted aryl, etc.; R2 = H, alkyl, (un)substituted aryl; R3 = halo, (un)substituted (hetero)aryl] were prepared Thus, reduction of N-benzylidene-[5-(2-chlorophenyl)-1H-pyrazolo[3,4-c]pyridazin-3-yl]amine with NaBH(OAc)3 in the presence of AcOH in THF afforded I [R1 = NHCH2Ph; R2 = H; R3 = 2-ClC6H4]. The compound I are claimed to be useful for the treatment and/or prophylaxis or conditions associated with a need for inhibition of GSK-3, such a diabetes, conditions associated with diabetes, chronic neurodegenerative conditions including such as Alzheimer's disease, Parkinson's disease, progressive supranuclear palsy, subacute sclerosing panencephalitic parkinsonism, postencephatilic parkinsonism, pugilistic encephalitics, guam parkinsonism-dementia complex, Pick's disease, corticobasal degeneration, frontotemporal dementia, Huntingdon's disease, AIDS associated dementia, amyotrophic lateral sclerosis, multiple sclerosis and neurotraumatic diseases such as acute stroke, mood disorders such as schizophrenia and bipolar disorders, promotion of functional recovery post stroke, cerebral bleeding (for example, due to solitary cerebral amyloid angiopathy), hair loss, obesity, atherosclerotic cardiovascular disease, hypertension, polycystic ovary syndrome, syndrome X, ischemia, traumatic brain injury, cancer, leukopenia, Down syndrome, Lewy body, inflammation, and immunodeficiency. The most potent compds. I show IC50 values in the range of 1 to 500 nM in GSK-3 assay. Pharmaceutical composition comprising the compound I was claimed.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

```
AN   2003:603894  CAPLUS
DN   139:149330
TI   Preparation of 4-oxo-butenoic acids and related compounds for the
     treatment of breast cancer
IN   Miles, Howard; Yurjevich, Solodnikov Sergey; Petrovna, Krasnykh Olga;
     Valentinovna, Pimenova Elena; Goun, Elena A.
PA   University of Central Florida, USA
SO   U.S., 15 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
PI   US 6602907        B1   20030805      US 2002-164541   20020607
                                          US 2001-296823PP 20010608
     US 6686496        B1   20040203      US 2002-165027   20020607
                                          US 2001-296823PP 20010608
     US 6638975        B1   20031028      US 2002-309619   20021204
                                          US 2001-296823PP 20010608
                                          US 2002-164541 A320020607
     US 6703426        B1   20040309      US 2002-309536   20021204
                                          US 2001-296823PP 20010608
                                          US 2002-164541 A320020607
     US 6713503        B1   20040330      US 2002-309718   20021204
                                          US 2001-296823PP 20010608
                                          US 2002-164541 A320020607
IT   572921-68-7P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (target compound; preparation of 4-oxo-butenoic acids and related compds.
for
        the treatment of breast cancer)
RN   572921-68-7  CAPLUS
CN   Benzenebutanoic acid, 2,3,5,6-tetrafluoro-4-methoxy-α,γ-dioxo-
     (9CI)  (CA INDEX NAME)
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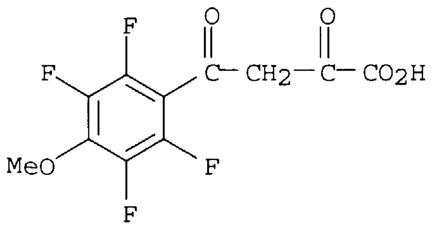

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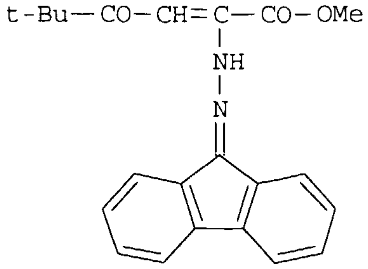
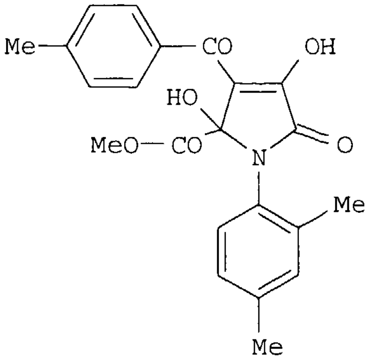


I



II

AB Title compds. I and II and related compds. are claimed useful for the treatment of breast carcinoma. For example, condensation of 2-hydroxy-5,5-dimethyl-4-oxohex-2-enoic acid Me ester and fluoren-9-ylidene hydrazine afforded claimed ester I in 68% yield. In human breast carcinoma cell growth inhibition and LD50 assays, 6-examples of 4-oxo-butenoic acids and related compds. exhibited 100% activity (sic) with LD50 values ranging from >200->3000 mg/kg., e.g., claimed ester I had 100% activity with LD50 value > 3000 mg/kg. Of note, 4-examples of 4-oxo-butenoic acids and related compds. posses at least "10 times lower acute toxicity compared to the most promising antitumor agent developed in the past three decades".

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:261816 CAPLUS
DN 138:287686
TI Preparation of water-soluble phenylpyridazine derivatives as IL-β inhibitors
IN Kyotani, Yoshinori; Koshi, Tomoyuki; Shigyo, Hiromichi; Yoshizaki, Hideo; Kitamura, Takahiro; Takemura, Shunji; Yasuoka, Kyoko; Totsuka, Junko; Sato, Seiichi
PA Kowa Co., Ltd., Japan
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 2

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     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
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PI   WO 2003027077        A1   20030403       WO 2002-JP9863   20020925
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
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US 2001-324569PP 20010926

PATENT FAMILY INFORMATION:

FAN 2004:3662

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004002497	A1	20040101	US 2003-396726	20030326
				US 2001-324569PP	20010926
				US 2002-253523 A2	20020925
	US 2003119838	A1	20030626	US 2002-253523	20020925
				US 2001-324569PP	20010926

OS MARPAT 138:287686

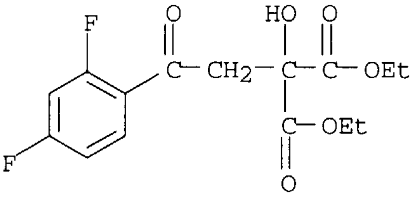
IT **503825-40-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of water-soluble phenylpyridazine derivs. as IL-β inhibitors)

RN 503825-40-9 CAPLUS

CN Propanedioic acid, [2-(2,4-difluorophenyl)-2-oxoethyl]hydroxy-, diethyl ester (9CI) (CA INDEX NAME)



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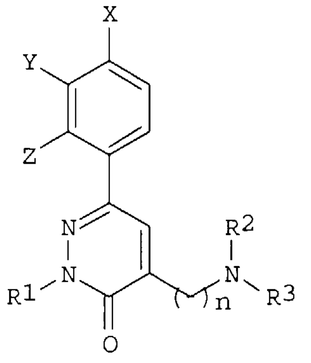

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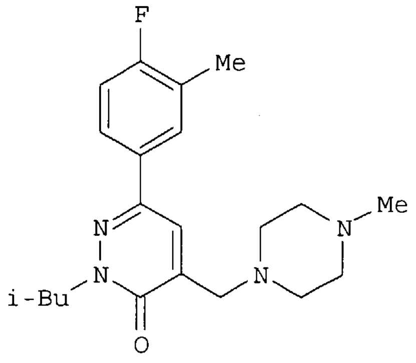

II

AB The title compds. I [wherein R1 = (un)substituted alkyl or alkenyl; R2 and R3 = independently H, alkyl, HO-alkyl, dihydroxyalkyl, or alkynyl; or R2 and R3 together form (un)substituted saturated heterocycle with the nitrogen atom attached; X, Y, and Z = independently H, halo, (un)substituted alkyl(thio), alkoxy, alkyl-SO, alkyl-SO2, or aryl; n = 1-5; with provisos] and their salts thereof are prepared as inhibitors of interleukin (IL) β production For example, the pyridazine II•2HCl was prepared in a multi-step synthesis in good yield. II•2HCl showed inhibiting activity with IC50 of 0.27 μM against IL-1β production in cow. I are highly soluble in water, and have a favorable oral absorbability.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:97391 CAPLUS
DN 138:137324
TI Preparation of phenylpropionic acid derivatives as α4 integrin inhibitors
IN Chiba, Akira; Sagi, Kazuyuki; Yoshimura, Toshihiko; Okuzumi, Tatsuya; Izawa, Hiroyuki; Murata, Masahiro
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

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     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
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PI   WO 2003010135      A1   20030206      WO 2002-JP7543    20020725
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                               JP 2001-225749 A 20010726
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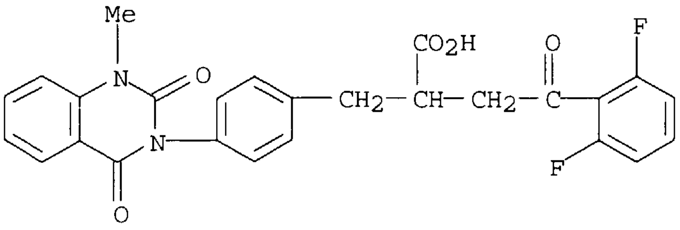
OS MARPAT 138:137324
IT **493004-41-4P**, 4-(2,6-Difluorophenyl)-2-[4-(1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxobutanoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)
RN 493004-41-4 CAPLUS
CN Benzenebutanoic acid, α-[[4-(1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)phenyl]methyl]-2,6-difluoro-γ-oxo- (9CI) (CA INDEX NAME)

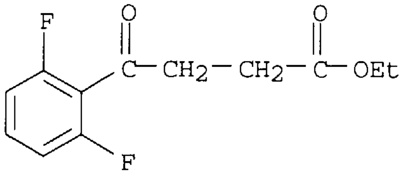


IT **493004-53-8P**, 4-(2,6-Difluorophenyl)-4-oxobutanoic acid ethyl ester

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenylpropionic acid derivs. as α4 integrin inhibitors for prevention or treatment of α4 integrin-participating various diseases)

RN 493004-53-8 CAPLUS

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, ethyl ester (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylpropionic acid derivs. represented by the general formula (I) [wherein A = Q-Q4, (un)substituted Ph, NR1-Z, NR1-CO-Z, NR1-SO2-Z, NR1-CONH-Z, NR1-C(:S)-NH-Z; wherein Z = (un)substituted Ph, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, cycloalkyl, etc.; R10-R17, R21, R22, R24, R25 = H, halo, OH, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; the ring Arm = benzene ring, cycloalkyl or aromatic ring containing 0, 1, 2,3, or 4 heteroatom(s) selected from O, S, and N;
R9, R20, R23 = O, (un)substituted NH, S; R18, R19 = H, lower alkyl, lower alkenyl, lower alkynyl, aryl, heteroaryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-lower alkenyl, or cycloalkyl-lower alkynyl optionally containing a heteroatoms in the cycloalkyl ring, etc.; B = HO, alkoxy, hydroxyl NH2, lower alkylamino; D = each (un)substituted lower alkyl, cycloalkylaryl optionally containing a heteroatoms in the ring, aryl, or heteroaryl; E = CO, CHOH; G-G1 = CH-CH2, C:CH; J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These derivs. exhibit α4 integrin inhibiting activity and are useful as therapeutic or preventive agents for various diseases in which α4 integrin participates, e.g., inflammatory diseases in which integrin-dependent adhesion participates. The above diseases include rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, cyclization of 4-oxo-4-phenylbutanoic acid in Ac2O at 90° gave 43% 5-phenyl-2,3-dihydrofuran-2-one which underwent condensation with 4-nitrobenzaldehyde in the presence of NaOAc in Ac2O at 80° for 1 h to give 93% 3-(4-nitrobenzylidene)-5-phenyl-2,3-dihydrofuran-2-one (II). Ring-opening methanolysis of II with NaOMe

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     in MeOH gave 84% 2-(4-nitrobenzylidene)-4-oxo-4-phenylbutanoic acid Me
     ester which was hydrogenated over 7.5% Pd/C in ethanol to give 28%
     2-(4-aminobenzyl)-4-oxo-4-phenylbutanoic acid Me ester (III).
     Cyclocondensation of III with 2-isocyanatobenzoic acid Me ester in MeCN at
     70° for 2 h and then at 70° for 11 h in the presence of Et3N
     gave 80% 2-[4-(2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl)benzyl]-4-oxo-4-
     phenylbutanoic acid Me ester (IV; R = X = H, R24 = Me) which was
     methylated by MeI in the presence of K2CO3 in DMF for 1 h to quant. give
     IV (R = R24 = Me, X = H).  Saponification of the latter compound with aqueous
LiOH in
     aqueous MeOH followed by acidification with 1 N aqueous HCl gave 54% IV (R =
Me,
     R24 = X = H).  IV (R = Me, R24 = X = H) and IV (R = Me, R24 = H, X = Cl)
     in vitro inhibited the binding of vascular cellular adhesion mol.-1
     (VCAM-1) to human B cell lymphoma cell expressing integrin α4β7
     with IC50 of ≤20 to <100 µmol/L and ≤0.9 µmol/L, resp.
RE.CNT  12    THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 8 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:964135  CAPLUS
DN   138:24543
TI   Preparation of benzyloxyphenyloxobutyrates and related compounds for the
     treatment of metabolic disorders
IN   Sharma, Shalini; Von Borstel, Reid W.; Hodge, Kirvin L.
PA   Wellstat Therapeutics Corporation, USA
SO   PCT Int. Appl., 242 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2002100341        A2   20021219      WO 2002-US18388  20020612
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                             US 2001-297282PP 20010612
     US 2003149107        A1   20030807      US 2002-167839   20020612
                                             US 2001-297282PP 20010612
     US 2004077896        A1   20040422      US 2003-684644   20031014
                                             US 2001-297282PP 20010612
                                             US 2002-167839 A320020612
OS   MARPAT 138:24543
IT   478162-62-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzyloxyphenyloxobutyrates and related compds. for
        treatment of metabolic disorders)
RN   478162-62-8  CAPLUS
```
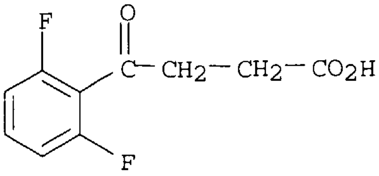
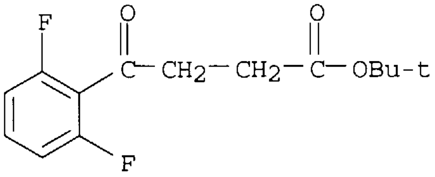
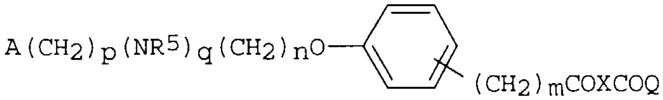

CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



IT **478163-14-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzyloxyphenyloxobutyrates and related compds. for treatment of metabolic disorders)
RN 478163-14-3 CAPLUS
CN Benzenebutanoic acid, 2,6-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



GI



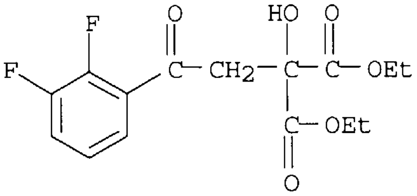
I

AB Biol. active title compds. [I; n = 1, 2; m, q, p = 0, 1; R5 = alkyl; R9 = H, halo, alkoxy; A = (halo-, alkyl-, perfluoromethyl-, alkoxy-, perfluoromethoxy-substituted) Ph, (Me-, Et-substituted) cycloalkyl, 5-6 membered heteroarom. ring having 1-2 N, S, O atoms; X = CH2, Q = OR1, R1 = Et; or X = CH2CR12R13, CH2CH(NHAc), Q = OR1, R1 = H, alkyl; or X = CH2CH2, Q = NR10R11; R12, R13 = H, Me; 1 of R10, R11 = H, alkyl, OH, the other = H, alkyl], were prepared Thus, 4-(2-fluorobenzyloxy)acetophenone (preparation given) in THF and DMPU was treated with a solution of Li bis(trimethylsilyl)amide at -60°; after 10 min, tert-Bu bromoacetate was added followed by stirring for an addnl. 10 min and warming to room temperature for 4 h to give tert-Bu 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyrate. The latter was stirred with CF3CO2H in CH2Cl2 to give 4-[4-(2-fluorobenzyloxy)phenyl]-4-oxobutyric acid. Tested I showed antidiabetic activity in a variety of tests. I are useful in treatment of various metabolic disorders such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis.

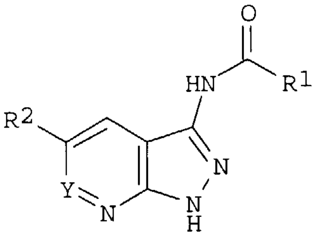
L7 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

GB 2001-7391 A 20010323
GB 2001-10671 A 20010501
GB 2001-12799 A 20010525
WO 2001-GB4186 W 20010919

OS MARPAT 136:263167
IT **405224-28-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolopyridines and pyrazolopyridazines as antidiabetics)
RN 405224-28-4 CAPLUS
CN Propanedioic acid, [2-(2,3-difluorophenyl)-2-oxoethyl]hydroxy-, diethyl ester (9CI) (CA INDEX NAME)



GI



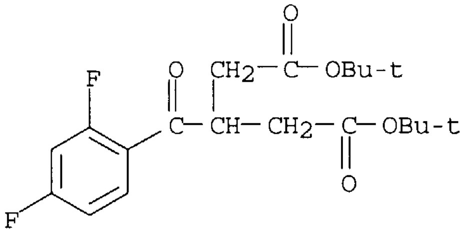
I

AB The title compds. [I; Y = CH, N; R1 = (un)substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R2 = unsubstituted aryl, (un)substituted heteroaryl], useful for the treatment of the condition associated with a need for the inhibition of GSK-3 such as diabetes, conditions associated with diabetes, and chronic neurodegenerative conditions, were prepared Thus, reacting butyryl chloride with 5-phenyl-1H-pyrazolo[3,4-b]pyridin-3-ylamine (preparation given) afforded I [Y = CH; R1 = Pr; R2 = Ph]. The most potent compds. I show IC50 values of 1-500 nM.

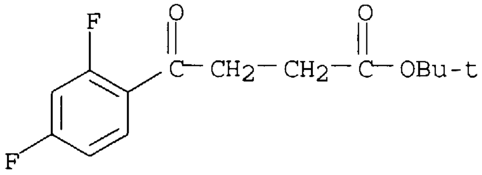
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:59018 CAPLUS
DN 136:262969
TI Synthesis of Mono- and Difluoronaphthoic Acids
AU Tagat, Jayaram R.; McCombie, Stuart W.; Nazareno, Dennis V.; Boyle, Craig D.; Kozlowski, Joseph A.; Chackalamannil, Samuel; Josien, Hubert; Wang, Yuguang; Zhou, Guowei
CS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA

SO Journal of Organic Chemistry (2002), 67(4), 1171-1177
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:262969
IT **405196-58-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(formation of dialkyl keto-ester in preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
RN 405196-58-9 CAPLUS
CN Pentanedioic acid, 3-(2,4-difluorobenzoyl)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



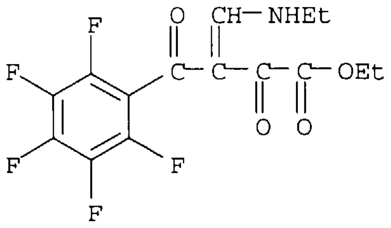
IT **405196-57-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluoronaphthoic acid from fluoroacetophenone via intramol. Friedel-Crafts cyclization/aromatization of fluorophenylbutanoyl chloride)
RN 405196-57-8 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



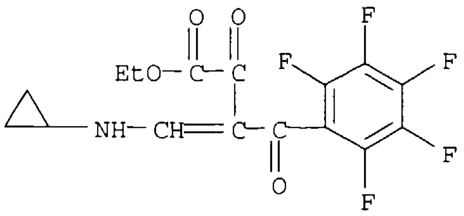
AB Aryl carboxamides are useful structural units found in several biol. active compds. Unlike their benzoic acid counterparts, fluorinated versions of naphthoic acids are relatively unknown. In connection with a recent project, we needed viable syntheses of several mono- and difluorinated naphthoic acids. Herein we describe the synthesis of 5-, 6-, 7-, and 8-fluoro-1-naphthalenecarboxylic acids and 5,7-, 5,8-, 6,7-, and 4,5-difluoro-1-naphthalenecarboxylic acids. The 5-fluoronaphthoic acid was obtained from the corresponding 5-bromo compound via electrophilic fluorination of the lithio-intermediate. The remaining 6-fluoro-, 7-fluoro-, 8-fluoro-, 5,7-difluoro-, 5,8-difluoro- and 6,7-difluoronaphthoic acids were prepared by a new, general route involving conversion of com. fluorinated phenylacetic acids to 2-(fluoroaryl)glutaric acids with differential ester groups; selective hydrolysis to a mono acid, intramol. Friedel-Crafts cyclization, and aromatization furnished the target structures. An alternative process to assemble a naphthalene skeleton is also presented for the 5,7-difluoro- and 5,8-difluoronaphthoic acids. Finally, 4,5-difluoro-1-naphthalenecarboxylic acid was prepared expeditiously from 1,8-diaminonaphthalene by adapting classical reactions.

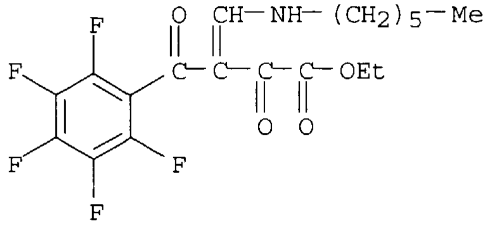
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:351596 CAPLUS
DN 135:210922
TI Synthesis of 2-(1-alkyl(aryl)-4-oxo-5,6,7,8-tetrafluoro-1,4-dihydroquinolin-3-yl)glyoxylic acid derivatives
AU Fokin, A. S.; Burgart, Y. V.; Saloutin, V. I.; Chupakhin, O. N.
CS Institute of Organic Synthesis, Urals Division, Russian Academy of Sciences, Yekaterinburg, 620219, Russia
SO Journal of Fluorine Chemistry (2001), 108(2), 187-194
CODEN: JFLCAR; ISSN: 0022-1139
PB Elsevier Science S.A.
DT Journal
LA English
OS CASREACT 135:210922
IT **312927-95-0P 312927-98-3P 312928-01-1P**
312928-04-4P 312928-06-6P 312928-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (oxotetrafluorodihydroquinolinyl)glyoxylates from pentafluorobenzoylpyruvate copper chelate via cyclization of (aminomethylene)pentafluorobenzoylpyruvates)
RN 312927-95-0 CAPLUS
CN Benzenebutanoic acid, β-[(ethylamino)methylene]-2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 312927-98-3 CAPLUS
CN Benzenebutanoic acid, β-[(cyclopropylamino)methylene]-2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)





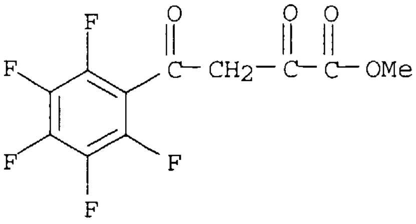
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I (R = Et, cyclopropyl, o-tolyl, H, Me, hexyl; R1 = H, Et) were prepared from the copper chelate of Et pentafluorobenzoylpyruvate via cyclocondensation of the (aminomethylene)pentafluorobenzoylpyruvates II. I (R = cyclopropyl, o-tolyl; R1 = Et) cyclized with o-phenylenediamine and o-aminophenol to give quinolinylquinoxalones and quinolinylbenzoxazines III (X = NH, O). I (R = o-tolyl) reacted with o-aminothiophenol to give the [(aminophenylthio)trifluoroquinolonyl](mercaptophenylimino)glyoxylate IV. Interaction of I (R = o-tolyl) and III (R = o-tolyl; X = NH) with morpholine gave 7-mono- and 5,7-disubstitution products depending on reaction conditions.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

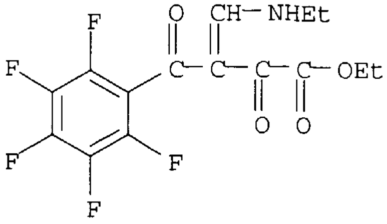
L7 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:771486 CAPLUS
DN 134:71456
TI Reaction of methyl pentafluorobenzoylpyruvate and its derivatives with 2-aminobenzenethiol
AU Saloutin, V. I.; Perevalov, S. G.; Chupakhin, O. N.
CS Institute of Organic Synthesis, Ural Division, Russian Academy of Sciences, Yekaterinburg, 620219, Russia
SO Russian Journal of Organic Chemistry (Translation of Zhurnal Organicheskoi Khimii) (2000), 36(5), 700-705
CODEN: RJOCEQ; ISSN: 1070-4280
PB MAIK Nauka/Interperiodica Publishing
DT Journal
LA English
OS CASREACT 134:71456
IT **314726-57-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reaction of Me pentafluorobenzoylpyruvate and its derivs. with aminobenzenethiol)
RN 314726-57-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, methyl ester (9CI) (CA INDEX NAME)



AB Transesterfication of bis(Et pentafluorobenzoylpyruvato)copper(II) gave bis(Me pentafluorobenzoylpyruvato)copper(II), which underwent intramol. cyclization to Me 5,6,7,8-tetrafluoro-4-oxochromene-2-carboxylate. Treatment of bis(Me pentafluorobenzoylpyruvato)copper(II) with hydrochloric acid afforded Me pentafluorobenzoylpyruvate which reacted with 2-aminobenzenethiol, yielding 2-[4-(2-aminophenylthio)tetrafluorophenyl]benzothiazole. The reaction of bis(Me pentafluorobenzoylpyruvato)copper(II) with 2-aminobenzenethiol hydrochloride resulted in formation of 3-pentafluorobenzoylmethylene-3,4-dihydro-2H-1,4-benzothiazin-2-one. Me 5,6,7,8-tetrafluoro-4-oxochromene-2-carboxylate reacted with 2-aminobenzenethiol to give product of replacement of the 7-fluorine atom by 2-aminophenylthio group.

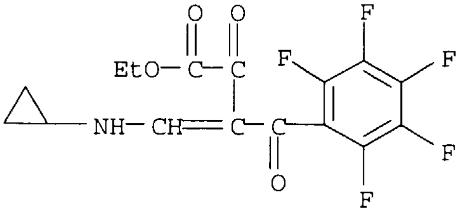
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:734292 CAPLUS
DN 134:42051
TI Synthesis of N-substituted 2-(5,6,7,8-tetrafluoro-4-oxo-1,4-dihydroquinolin-3-yl)glyoxylic acids
AU Obanin, G. A.; Fokin, A. S.; Burgart, Ya. V.; Ryzhkov, O. V.; Skryabina, Z. E.; Saloutin, V. I.; Chupakhin, O. N.
CS Institute of Organic Synthesis, Ural Division of the Russian Academy of Sciences, Yekaterinburg, 620219, Russia
SO Russian Chemical Bulletin (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya) (2000), 49(7), 1231-1236
CODEN: RCBUEY; ISSN: 1066-5285
PB Consultants Bureau
DT Journal
LA English
OS CASREACT 134:42051
IT **312927-95-0P 312927-98-3P 312928-01-1P**
312928-04-4P 312928-06-6P 312928-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (tetrafluorooxodihydroquinoline)glyoxylates via amination of pentafluorobenzoylpyruvate-orthoformate condensation product)
RN 312927-95-0 CAPLUS
CN Benzenebutanoic acid, β-[(ethylamino)methylene]-2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



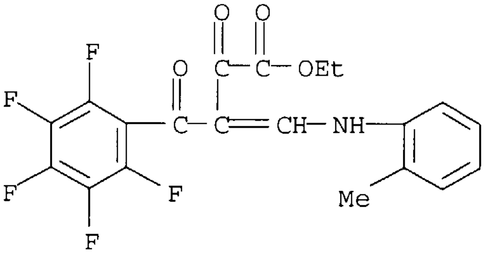
RN 312927-98-3 CAPLUS

CN Benzenebutanoic acid, β-[(cyclopropylamino)methylene]-2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



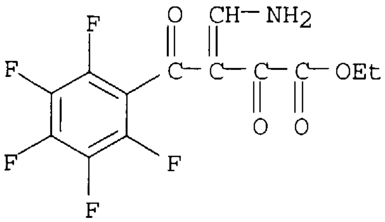
RN 312928-01-1 CAPLUS

CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-β-[[(2-methylphenyl)amino]methylene]-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



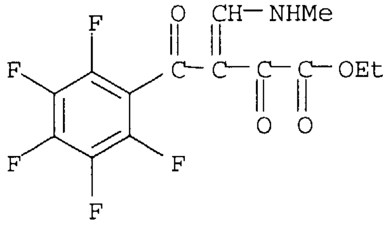
RN 312928-04-4 CAPLUS

CN Benzenebutanoic acid, β-(aminomethylene)-2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

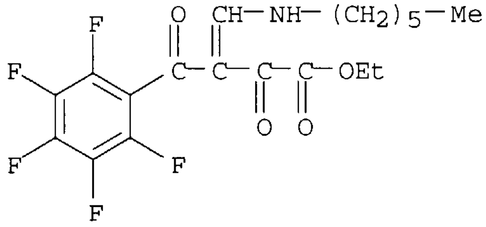


RN 312928-06-6 CAPLUS

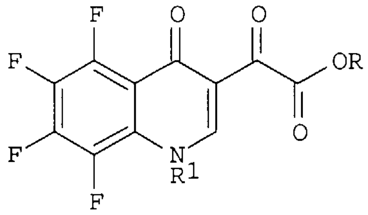
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-β-[(methylamino)methylene]-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 312928-08-8 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-β-[(hexylamino)methylene]-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



GI



I

AB The title compds. I (R = H, Et; R1 = Et, cyclopropyl, 2-MeC6H4, H, Me, hexyl) were prepared from the Cu chelate of Et (pentafluorobenzoyl)pyruvate by successive condensation with HC(OEt)3/Ac2O and R1NH2. The mol. structures of intermediate Et 4-amino-2-oxo-3-pentafluorobenzoylbut-3-enolates were discussed.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:522602 CAPLUS
DN 131:286470
TI Synthesis of fluorine-containing 3-arylhydrazo-2,3,4-triketoesters and their heterocyclization
AU Saloutin, V. I.; Fokin, A. S.; Burgart, Ya. V.

CS Institute of Organic Chemistry, Ural Division, Russian Academy of Sciences, Yekaterinburg, Russia

SO Russian Journal of Organic Chemistry (Translation of Zhurnal Organicheskoi Khimii) (1999), 35(2), 290-295
CODEN: RJOCEQ; ISSN: 1070-4280

PB MAIK Nauka/Interperiodica Publishing

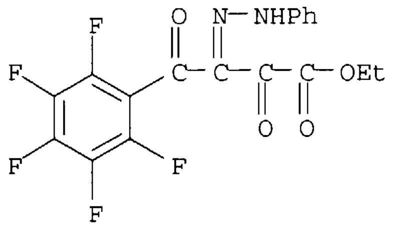
DT Journal

LA English

IT **220205-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of (arylhydrazo) fluoro keto esters)

RN 220205-88-9 CAPLUS

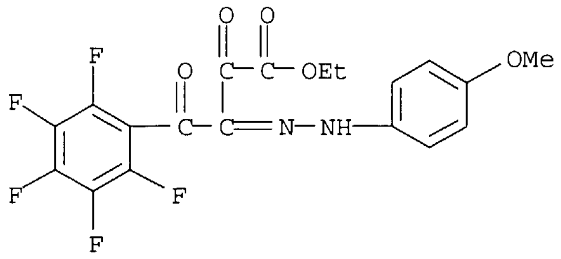
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-β-(phenylhydrazono)-, ethyl ester (9CI) (CA INDEX NAME)



IT **220205-89-0P 220205-91-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

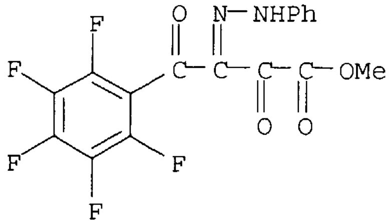
RN 220205-89-0 CAPLUS

CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-β-[(4-methoxyphenyl)hydrazono]-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 220205-91-4 CAPLUS

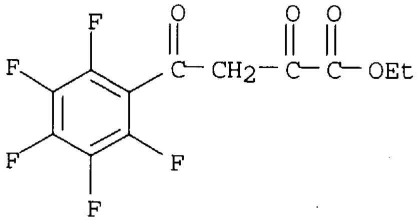
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-β-(phenylhydrazono)-, methyl ester (9CI) (CA INDEX NAME)



AB 3-Arylhydrazones of fluorine-containing 2,3,4-triketoesters were prepared for the first time by coupling of aryldiazonium chlorides with esters of fluoroacyl(aroyl)pyruvic acids and their chelates. Reactions of the arylhydrazones with hydrazine hydrate and o-phenylenediamine result in substituted pyrazoles and quinoxalines resp. Intramol. cyclization of fluoroaroyl pyruvate arylhydrazones and derivs. thereof provides new possibilities of synthesis of heterocycles from cinnoline series.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:319066 CAPLUS
DN 131:170318
TI Reactions of pentafluorobenzoylpyruvic ester and its copper(II) chelate with dinucleophiles
AU Saloutin, V. I.; Perevalov, S. G.
CS Urals Division, Institute of Organic Synthesis, Russian Academy of Sciences, Yekaterinburg, 620219, Russia
SO Journal of Fluorine Chemistry (1999), 96(1), 87-93
CODEN: JFLCAR; ISSN: 0022-1139
PB Elsevier Science S.A.
DT Journal
LA English
IT **161037-54-3**, Ethyl (pentafluorobenzoyl)pyruvate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of (fluorobenzoyl)pyruvate and its copper(II) chelate with dinucleophiles)
RN 161037-54-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



AB (Pentafluorobenzoyl)pyruvic ester reacts with dinucleophiles (hydrazine, phenylhydrazine, hydroxylamine hydrochloride, 1,2-ethylenediamine, 1,2-phenylenediamine, 2-aminophenol) to form heterocyclic compds. Reactions between bis[Et (pentafluorobenzoyl)pyruvate]copper(II) chelate and these amine hydrochlorides also produce heterocycles.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

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          ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 18 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:222909  CAPLUS
DN   130:237373
TI   Preparation of 2-aminotetralines for the prevention and treatment of
     inflammatory and/or autoimmune pathologies.
IN   Fanto, Nicola; Moretti, Gian Piero; Foresta, Piero
PA   Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SO   PCT Int. Appl., 69 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9915494         A1   19990401      WO 1998-IT252     19980922
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
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IT 1997-RM568 A 19970922
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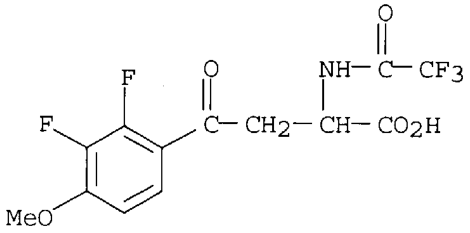
US 2001-816317 A320010326

OS MARPAT 130:237373

IT **221385-03-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-aminotetralines for the prevention and treatment of inflammatory and/or autoimmune pathologies)

RN 221385-03-1 CAPLUS

CN Benzenebutanoic acid, 2,3-difluoro-4-methoxy-γ-oxo-α-[(trifluoroacetyl)amino]- (9CI) (CA INDEX NAME)



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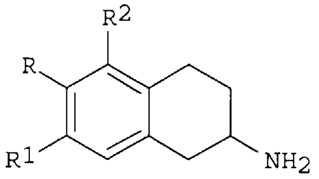

I

AB Title compds. [I; R, R1 = halo, OH, (substituted) alkoxy, alkanoyl, alkyl, carbamoyl, carbamoyloxy, amino, etc.; R2 = H, halo, OH, MeO; with provisos], and salts thereof, were prepared Thus, (R)-(+)-2-amino-6-fluoro-7-hydroxytetralin hydrochloride (prepared in several steps from D-aspartic acid and 2-fluoroanisole) at 18 mg/kg i.v. improved survival in E. coli LPS-treated mice by 44%.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:708308 CAPLUS

DN 130:168314

TI Synthesis of fluorinated 2(3)-arylhydrazones of 1,2,3-tri(1,2,3,4-tetra)carbonyl compounds and their heterocyclization reactions

AU Burgart, Y. V.; Fokin, A. S.; Kuzueva, O. G.; Chupakhin, O. N.; Saloutin, V. I.

CS Urals Division, Institute of Organic Synthesis, Russian Academy of Sciences, Yekaterinburg, 620219, Russia

SO Journal of Fluorine Chemistry (1998), 92(2), 101-108
CODEN: JFLCAR; ISSN: 0022-1139

PB Elsevier Science S.A.
DT Journal
LA English
OS CASREACT 130:168314
IT **220205-88-9P 220205-89-0P 220205-90-3P**
220205-91-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and heterocyclization of fluorinated arylhydrazones of tri(tetra)carbonyl compds.)
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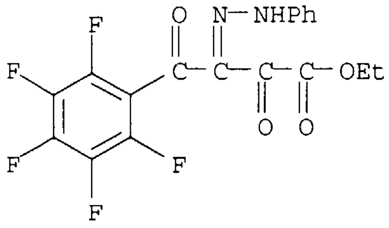

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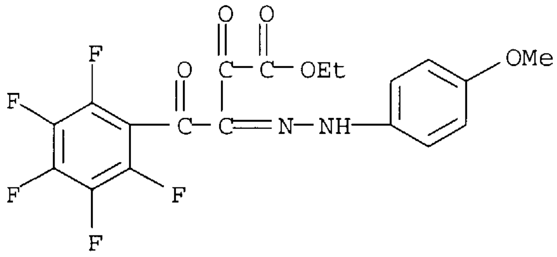

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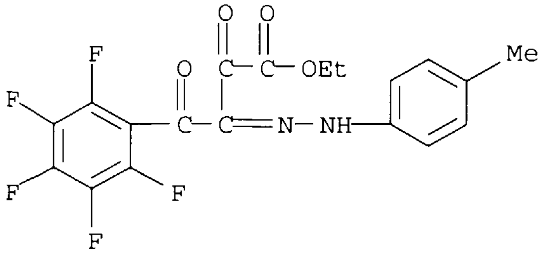

RN 220205-91-4 CAPLUS
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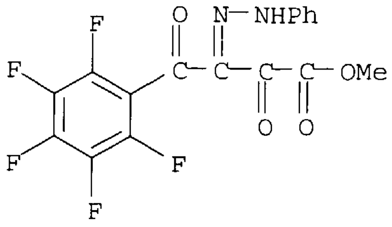

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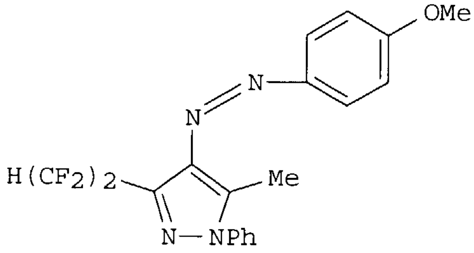

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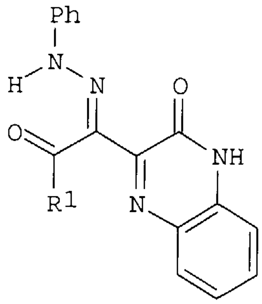

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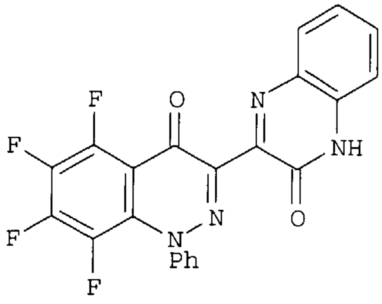
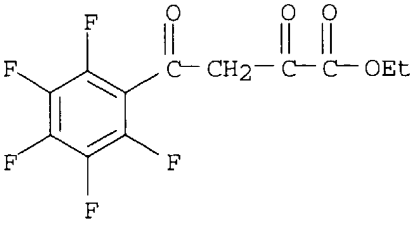


III

AB New fluorinated 2-arylhydrazones of 1,2,3-triketones, 2-arylhydrazone-1,2,3-diketo esters and 3-arylhydrazone-1,2,3,4-triketo esters have been prepared by the coupling of fluorine-containing 1,3-keto esters, 1,3-diketones, acyl(aroyl)pyruvic esters and their chelates with aryldiazonium chlorides. The arylhydrazones react with hydrazine hydrate, phenylhydrazine, thiosemicarbazide and hydroxylamine to form the corresponding pyrazole and isoxazole derivs, e.g., I. Interaction of 3-arylhydrazone-1,2,3,4-diketo esters with o-phenylenediamine results in quinoxaline products II (R1 = CF3, Ph). Intramol. cyclization of the arylhydrazones with pentafluorophenyl substituents leads to cinnolone derivative III.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT



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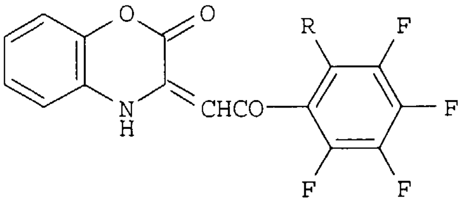

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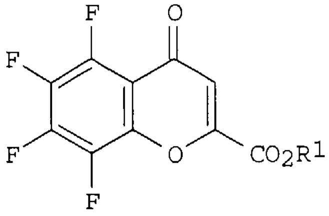
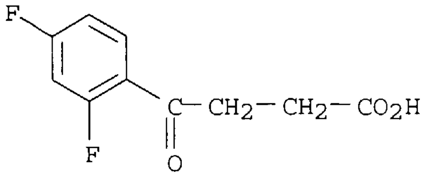


II

AB Cyclocondensation of Et (pentafluorobenzoyl)pyruvate and its Cu(II) enolate with o-aminophenol gave benzoxazinone I (R = F). Chromones II (R1 = Et, H) reacted with o-aminophenol to give I (R = OH).

L7 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:50386 CAPLUS
DN 126:152347
TI The measurement of molecular diversity: a three-dimensional approach
AU Chapman, David
CS Afferent Systems Inc., San Francisco, CA, 94114, USA
SO Journal of Computer-Aided Molecular Design (1996), 10(6), 501-512
CODEN: JCADEQ; ISSN: 0920-654X
PB ESCOM
DT Journal
LA English
IT **110931-77-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(measurement of mol. diversity in terms of factors relevant to ligand-protein binding: application to carboxylates)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



AB This paper describes a method for selecting a small, highly diverse subset from a large pool of mols. The method has been employed in the design of combinatorial synthetic libraries for use in high-throughput screening for pharmaceutical lead generation. It computes diversity in terms of the main factors relevant to ligand-protein binding, namely the three-dimensional arrangement of steric bulk and of polar functionalities and mol. entropy. The method was used to select a set of 20 carboxylates suitable for use as side-chain precursors in a polyamine-based library. The method depends on ests. of various phys.-chemical parameters involved in ligand-protein binding; expts. examined the sensitivity of the method to these parameters. This paper compares the diversity of randomly and rationally selected side-chain sets; the results suggest that careful design of synthetic combinatorial libraries may increase their effectiveness several-fold.

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L7   ANSWER 23 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1996:524249  CAPLUS
DN   125:195657
TI   Benzocycloalkylazolethione derivatives useful as dopamine
     β-hydroxylase inhibitors.
IN   Martinez, Gregory R.; Gooding, Owen W.; Repke, David B.; Teitelbaum,
     Philip J.; Walker, Keith A. M.; Whiting, Roger L.
PA   USA
SO   U.S., 55 pp., Cont.-in-part of U.S. Ser. No. 233,835, abandoned.
     CODEN: USXXAM
DT   Patent
LA   English
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OS MARPAT 125:195657

IT **170151-15-2P**

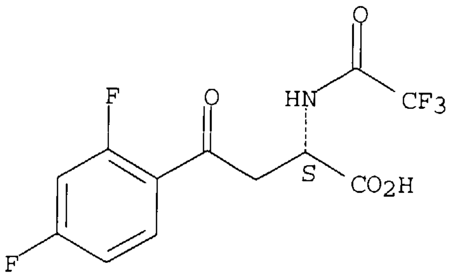
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of benzocycloalkylazolethione derivs. as dopamine β-hydroxylase inhibitors)

RN 170151-15-2 CAPLUS

CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-[(trifluoroacetyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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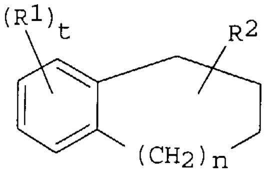

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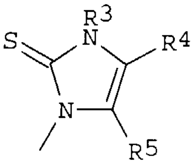

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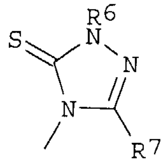

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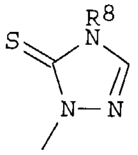
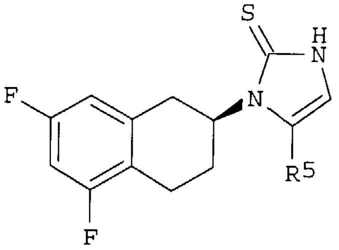


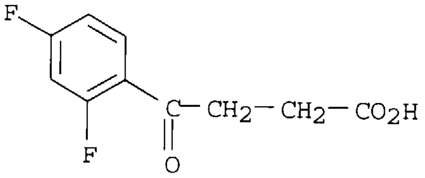


II

AB The invention relates to novel benzocycloalkylazolethiones I [n = 0-2; t = 0-3; R1 = halo, OH, alkoxy; R2 = imidazole group Q1 or triazole group Q2 or Q3; R3 = H, (un)substituted NH2, (CH2)qR9, etc.; q = 0-4; R4 = H, , alkyl, CO2H, carbamoyl, etc.; R5 = H, (un)substituted NH2, etc.; R6 = H, CH2CH2CO2H, CH2CH2CONH2, etc.; R7 = H, (un)substituted CH2NH2; R8 = groups given for R6, or (un)substituted NH2; R9 = CO2H or derivs., (un)substituted aryl or heteroaryl, etc.] and related compds. The compds. are are dopamine β-hydroxylase inhibitors, and are thus peripheral vasodilators useful in the treatment of hypertension and congestive heart failure (no data). For example, (S)-5,7-difluoro-1,2,3,4-tetrahydronaphthalen-2-ylamine-HCl [preparation given] reacted with formaldehyde-Na bisulfite complex and KCN to give the N-(cyanomethyl) derivative, which underwent N-formylation with HCO2Bu, α-condensation with HCO2Et, and cyclization with KSCN, to give title compound II [R5 = cyano]. This was reduced with LiAlH4 in THF to give II [R5 = CH2NH2].

L7 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:487408 CAPLUS
DN 125:275746
TI Concise asymmetric routes to 2,2,4-trisubstituted tetrahydrofurans via

chiral titanium imide enolates: key intermediates towards synthesis of highly active azole antifungals Sch 51048 and Sch 56592
AU Saksena, Anil K.; Girijavallabhan, Viyyoor M.; Wang, Haiyan; Liu, Yi-Tsung; Pike, Russell E.; Ganguly, Ashit K.
CS Schering-Plough Res. Inst., Kenilworth, NJ, 07033, USA
SO Tetrahedron Letters (1996), 37(32), 5657-5660
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 125:275746
IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of tetrahydrofurans as Sch 51048 and 56592 intermediates via chiral titanium imide enolates)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)



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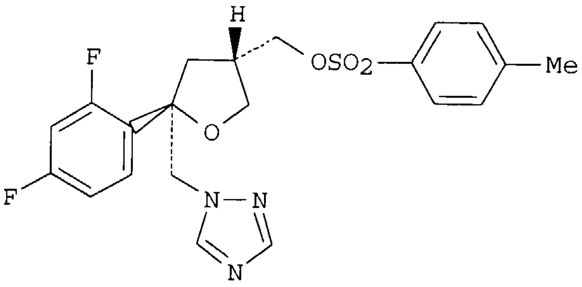

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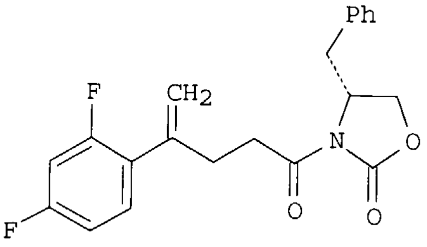

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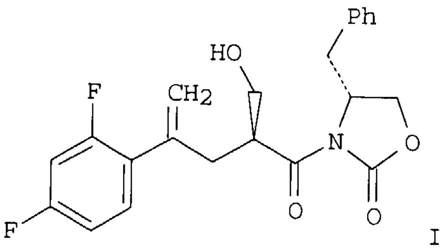

III

AB Two complimentary approaches to the key (-)-(2R)-cis-tosylate I and its (+)-(2S)-enantiomer via generation of chiral imide enolates having a 2,2-disubstituted olefin functionality in the β-position, are described. In a "protecting group free" sequence, reaction of the titanium enolate generated from (4R)-benzyl-2-oxazolidinone derived imide II with s-trioxane provided a convenient oxazolidinone intermediate III which could be directly subjected to 2,4-diastereoselective iodocycln.

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L7   ANSWER 25 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1996:252221  CAPLUS
DN   124:289531
TI   Preparation of pyrazole derivatives as herbicides
IN   Nebel, Kurt; Brunner, Hans-Georg; Pissiotas, Georg
PA   Ciba-Geigy A.-G., Switz.
SO   PCT Int. Appl., 202 pp.
     CODEN: PIXXD2
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LA   English
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OS   MARPAT 124:289531
IT   175711-74-7P
     RL: AGR (Agricultural use); BAC (Biological activity or effector, except
     adverse); BSU (Biological study, unclassified); SPN (Synthetic
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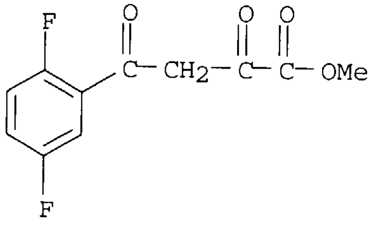
preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazole derivs. as herbicides)

RN 175711-74-7 CAPLUS

CN Benzenebutanoic acid, 2,5-difluoro-α,γ-dioxo-, methyl ester (9CI) (CA INDEX NAME)



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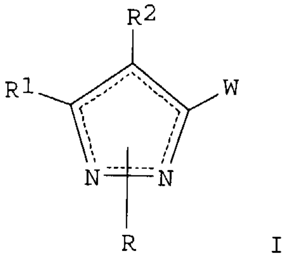

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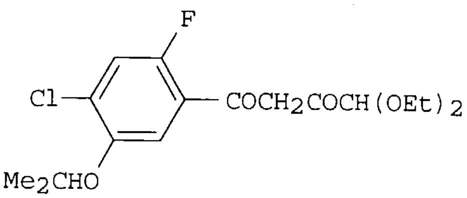

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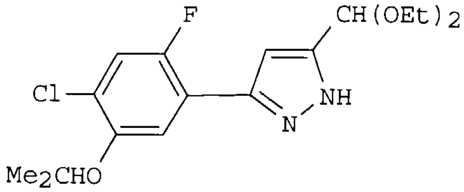

III

AB Pyrazole derivs. [I; R = H, C1-6 alkyl, C3-8 cycloalkyl, etc.; R1 = cyano, halocarbonyl, alkoxycarbonyl, (un)substituted carbamoyl, etc.; R2 = H, halo, C1-4 alkyl, C3-6 cycloalkyl, etc.; W = (un)substituted aryl], their N-oxides, salts, and complexes are prepared N2H4.H2O was added dropwise to a solution of diketone II in EtOH with stirring at room temperature and the solution
refluxed to give pyrazole III. Some I showed complete control of Setaria, Solanum, etc. at 2 kg/ha.

L7 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:998191 CAPLUS

DN 124:176116

TI Preparation of benzocycloalkylazolethione derivatives as dopamine β-hydroxylase inhibitors.

IN Martinez, Gregory R.; Repke, David B.; Teitelbaum, Philip J.; Walker, Keith A. M.; Gooding, Owen W.; Whiting, Roger L.; Bansal, Rekha P.;

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         Muehldorf, Alexander V.; O'yang, Counde
PA       Syntex (U.S.A.) Inc., USA
SO       PCT Int. Appl., 146 pp.
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OS   MARPAT 124:176116
IT   170151-15-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of benzocycloalkylazolethione derivs. as dopamine
        β-hydroxylase inhibitors)
RN   170151-15-2  CAPLUS
CN   Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-
     [(trifluoroacetyl)amino]-, (S)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (+).
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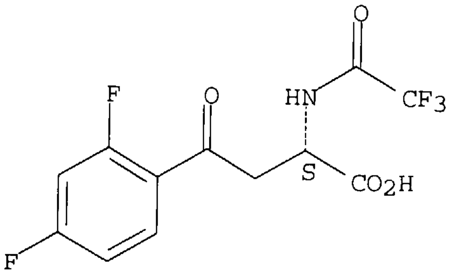

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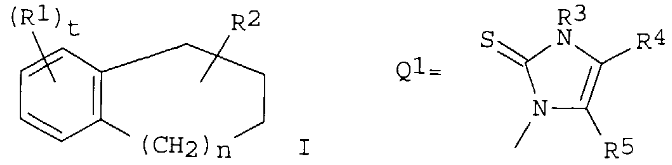
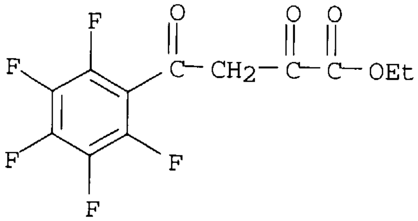


AB Title compds. [I; n = 0-2; t = 0-3; q = 0-4; R1 = halo, OH, alkyloxy; R2 = Q1, etc.; R3 = H, amino, (CH2)qR9; R4 = H; R5 = H, amino, acylamino; R9 = CO2H, alkoxycarbonyl, carbamoyl, (substituted) aryl, heteroaryl; with provisos] were prepared as dopamine β-hydroxylase inhibitors. Thus, (S)-5-aminomethyl-1-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione hydrochloride (preparation given) at 10 mg/kg in rats reduced mean arterial blood pressure by 53 mm Hg.

L7 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:932936 CAPLUS
DN 124:117239
TI Reaction of copper chelates of (polyfluoroacyl)pyruvic acid esters with hydrazine and o-phenylenediamine
AU Saloutin, V. I.; Skryabina, Z. E.; Kondrat'ev, P. N.; Perevalov, S. G.
CS Inst. Org. Sint., Ural. Otd. RAN, Yekaterinburg, Russia
SO Zhurnal Organicheskoi Khimii (1995), 31(2), 266-9
CODEN: ZORKAE; ISSN: 0514-7492
PB Nauka
DT Journal
LA Russian
IT **161037-54-3**, Ethyl (pentafluorobenzoyl)pyruvate
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation with hydrazine and phenylenediamine)
RN 161037-54-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



AB Polyfluorinated derivs. of pyrazolecarboxylates and quinoxalinones were prepared by the title reactions.

L7 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:896100 CAPLUS
DN 123:313934
TI Preparation of 2(5H)-furanones, 2(5H)-thiophenones, 2(5H)-pyrrolones and benzodioxolyls as endothelin antagonists
IN Berryman, Kent Alan; Doherty, Annette Marian; Edmunds, Jeremy John; Patt, William Chester; Plummer, Mark Stephen; Repine, Joseph Thomas
PA Warner-Lambert Co., USA

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SO   PCT Int. Appl., 423 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
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PI   US 5691373         A    19971125      US 1995-384083    19950206
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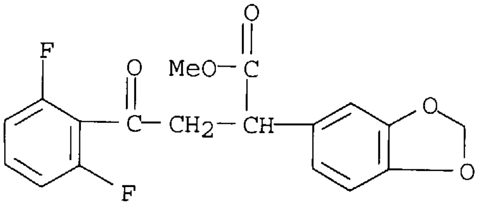
OS MARPAT 123:313934
IT **169803-96-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2(5H)-furanones, 2(5H)-thiophenones, 2(5H)-pyrrolones and benzodioxolyls as endothelin antagonists)
RN 169803-96-7 CAPLUS
CN 1,3-Benzodioxole-5-acetic acid, α-[2-(2,6-difluorophenyl)-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)



AB Title compds. and salts thereof are prepared Chalcones were treated with KCN to give nitrile addition products, hydrolysis of which gave the corresponding acids which were then cyclized with aldehydes give 2(5H)-furanones. In vitro and in vivo antagonism was demonstrated. Title compds. are claimed for many human diseases in which endothelin is involved.

L7 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:846347 CAPLUS
DN 124:55777
TI Synthesis of 2(3)-(ethoxycarbonyl)-5,6,7,8-tetrafluorochromones
AU Saloutin, V. I.; Skryabina, Z. E.; Bazyl, I. T.; Chupakhin, O. N.
CS Inst. Org. Chem., Ural Br. Russ. Acad. Sci., Yekaterinburg, 620219, Russia
SO Izvestiya Akademii Nauk, Seriya Khimicheskaya (1993), (2), 362-4
CODEN: IASKEA
PB Nauka
DT Journal
LA Russian
OS CASREACT 124:55777
IT **161037-54-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of (ethoxycarbonyl)tetrafluorochromes)

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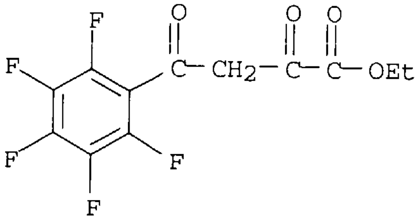
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



AB The hitherto unknown Et pentafluorobenzoylpyruvate was prepared by condensing pentafluoroacetophenone with di-Et oxalate. Intramol. cyclization of this ester or its Cu(II), and of Et 2-ethoxymethylenepentafluorobenzoylacetate affords novel 2- and 3-ethoxycarbonyl-5,6,7,8-tetrafluorochromones. Hydrolysis of the latter followed by decarboxylation gives 5,6,7,8-tetrafluorochrome.

L7 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:773022 CAPLUS
DN 123:313966
TI Process for making 1-benzocycloalkyl-1,3-dihydroimidazole-2-thione derivatives via cyclization of benzocycloalkylamines with thiocyanic acid and dihydroxyacetone
IN Bansal, Rekha P.; Gooding, Owen W.; Muehldorf, Alexander V.; O-Yang, Counde
PA Syntex (U.S.A.) Inc., USA
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
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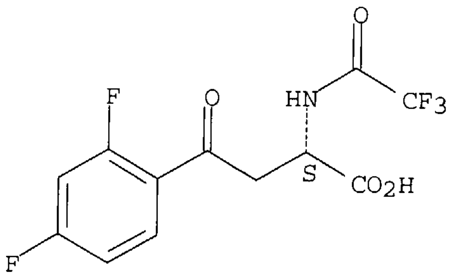
FI 9604312	A	19961220	FI 1996-4312 19961025
			US 1994-233655 A 19940426
			US 1994-233835 A 19940426
			US 1995-403209 A 19950317
			WO 1995-US4783 W 19950425
NO 9604552	A	19961227	NO 1996-4552 19961025
			US 1994-233655 A 19940426
			US 1994-233835 A 19940426
			US 1995-403209 A 19950317
			WO 1995-US4783 W 19950425
US 5719280	A	19980217	US 1997-833560 19970407
			US 1994-233655 A219940426
			US 1995-403209 A319950317
			US 1996-639387 B119960429
AU 9740994	A1	19980108	AU 1997-40994 19971014
AU 700600	B2	19990107	
			US 1994-233655 A 19940426
			US 1994-233835 A 19940426
			US 1995-403209 A 19950317

OS CASREACT 123:313966; MARPAT 123:313966
IT **170151-15-2P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-benzocycloalkyl-1,3-dihydroimidazole-2-thione derivs. via cyclization of benzocycloalkylamines with thiocyanic acid and dihydroxyacetone)
RN 170151-15-2 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo-α-[(trifluoroacetyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to a process for preparing an acid addition salt of title compds. I in which: n is 0, 1 or 2; m is 0, 1, 2 or 3; R1 is independently halo, hydroxy or (C1-4)alkyloxy; or the free base, an individual stereoisomer, or a mixture of stereoisomers thereof, which process comprises (A) reacting a benzocycloalkylamine II with thiocyanic acid and dihydroxyacetone to give a corresponding 5-hydroxymethyl-1-benzocycloalkyl-1,3-dihydroimidazole-2-thione III and then (B) reacting III with a compound of the formula H2NCOR2 or an ammonium salt of the formula NH4+-OC(O)R2 [in which R2 is hydrogen, (C1-4)alkyl or trifluoro(C1-4)alkyl] to give IV; and (C) hydrolyzing IV with acid; and (D) optionally reacting the acid addition salt of I with an inorg. or organic base to give the corresponding free base form; and (E) optionally reacting the free base form of I with a pharmaceutically acceptable acid to give the corresponding acid addition salt; and (F) optionally separating a mixture of stereoisomers of a I to give a single stereoisomer. Thus, e.g., acylation of 1,3-difluorobenzene with N-(trifluoroacetyl)-L-aspartic anhydride afforded (S)-2-[(trifluoroacetyl)amino]-4-(2,4-difluorophenyl)-4-oxobutanoic acid; hydrogenation of the latter afforded (S)-2-[(trifluoroacetyl)amino]-4-(2,4-difluorophenyl)butanoic acid; cyclization of the latter afforded (S)-5,7-difluoro-2-[(trifluoroacetyl)amino]-3,4-dihydro(2H)-naphthalen-1-one which upon hydrogenation and hydrolysis afforded (S)-5,7-difluoro-1,2,3,4-tetrahydronaphthalen-2-ylamine hydrochloride [(S)-II with n = 1, m = 2, R1 = 5,7-F2]; the latter was converted to (S)-5-Hydroxymethyl-1-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione (III)

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     with potassium thiocyanate/dihydroxyacetone; reaction of III with
     formamide afforded (S)-N-[3-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-2-
     yl)-2-thioxo-2,3-dihydro-1H-imidazol-4-ylmethyl]formamide (IV); treatment
     of IV with concentrated HCl afforded (S)-5-aminomethyl-1-(5,7-difluoro-1,2,3,4-
     tetrahydronaphthalen-2-yl)-1,3-dihydroimidazole-2-thione hydrochloride
     (I.HCl).

L7   ANSWER 31 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1995:682560  CAPLUS
DN   123:112065
TI   Preparation of chiral 2-azolylmethyl-2-phenyl-4-
     sulfonyloxymethyltetrahydrofurans as antifungal intermediates
IN   Saksena, Anil K.; Girijavallabhan, Viyyoor M.; Pike, Russell E.; Wang,
     Haiyan; Lovey, Raymond G.; Liu, Yi-Tsung; Ganguly, Ashit K.; Morgan,
     William Brian; Zaks, Aleksey
PA   Schering Corp., USA
SO   PCT Int. Appl., 67 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.       KIND  DATE           APPLICATION NO.  DATE
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             US, UZ, VN
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                                           US 1993-55268  A 19930430
     US 5403937        A    19950404       US 1993-55268    19930430
     CA 2161662        AA   19941110       CA 1994-2161662  19940428
     CA 2161662        C    20010102
                                           US 1993-55268  A 19930430
     AU 9466671        A1   19941121       AU 1994-66671    19940428
     AU 681659         B2   19970904
                                           US 1993-55268  A 19930430
                                           WO 1994-US4355 W 19940428
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     EP 696282         B1   19990714
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
                                           US 1993-55268  A 19930430
                                           WO 1994-US4355 W 19940428
     CN 1122134        A    19960508       CN 1994-191958   19940428
     CN 1057089        B    20001004
                                           US 1993-55268  A 19930430
     HU 73760          A2   19960930       HU 1995-3084     19940428
     HU 219143         B    20010228
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     JP 08509730       T2   19961015       JP 1994-524378   19940428
     JP 3411283        B2   20030526
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     AT 182146         E    19990715       AT 1994-915399   19940428
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     ES 2133559        T3   19990916       ES 1994-915399   19940428
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                                               WO 1994-US4355   W 19940428
      PL 182328          B1    20011231        PL 1994-311267     19940428
                                               US 1993-55268    A 19930430
                                               WO 1994-US4355   W 19940428
      FI 9505119         A     19951027        FI 1995-5119       19951027
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                                               WO 1994-US4355   W 19940428
      NO 9504314         A     19960102        NO 1995-4314       19951027
                                               US 1993-55268    A 19930430
                                               WO 1994-US4355   W 19940428
      HK 1008822         A1    20000414        HK 1998-109521     19980729
                                               US 1993-55268    A 19930430
                                               WO 1994-US4355   W 19940428
OS    MARPAT 123:112065
IT    110931-77-6P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation of chiral 2-azolylmethyl-2-phenyl-4-
         sulfonyloxymethyltetrahydrofurans as antifungal intermediates)
RN    110931-77-6  CAPLUS
CN    Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI)  (CA INDEX NAME)
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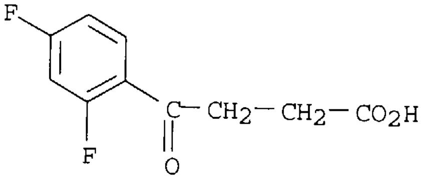

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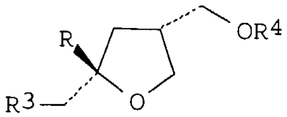

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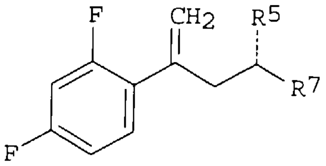
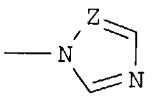


II

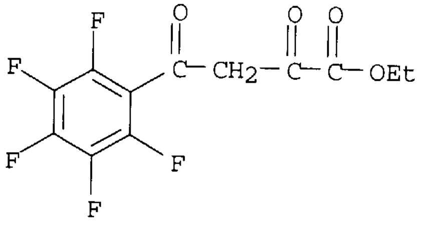
Q=



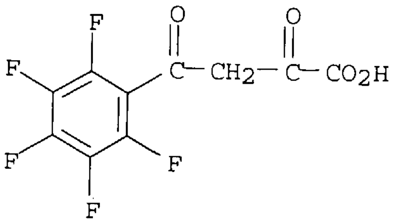
AB   Title compds. [I; R = 2,4-R1R2C6H3; R1,R2 = F or Cl; R3 = azolo group Q; R4 = OSO2R6; R6 = CF3, alkyl, (un)substituted aryl; Z = CH or N] were prepared 2,4-F2C6H3C(:CH2)CH2OH was converted in 2 steps to intermediate II [R5 = H; R7 = (S)-4-isopropyl-2-oxazolidinonocarbonyl] which was treated with TiCl4/Et3N/ClCH2OCH2Ph and the product reduced to give II (R5 = CH2OCH2Ph, R7 = CH2OH). The latter was treated with iodine to give I (R =

2,4-F2C6H3, R3 = iodo, R4 = CH2Ph) which was converted in 2 steps to I (R = 2,4-F2C6H3, R3 = Q, R4 = Ts, Z = N).

L7 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:541990 CAPLUS
DN 123:198592
TI Reaction of (pentafluorobenzoyl)pyruvic acid with amines
AU Saloutin, V. I.; Bazyl', I. T.; Skryabina, Z. E.; Kondrat'ev, P. N.; Chupakhin, O. N.
CS Inst. Org. Synth., Ural Branch Russian Acad. Sci., Ekaterinburg, 620219, Russia
SO Izvestiya Akademii Nauk, Seriya Khimicheskaya (1994), (2), 299-302
CODEN: IASKEA
PB Institut Organicheskoi Khimii im. N. D. Zelinskogo Rossiiskoi Akademii Nauk
DT Journal
LA Russian
IT **161037-54-3**, Ethyl (pentafluorobenzoyl)pyruvate
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of)
RN 161037-54-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

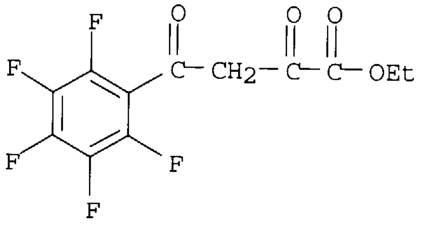


IT **162188-41-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reaction of (pentafluorobenzoyl)pyruvic acid with amines)
RN 162188-41-2 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo- (9CI) (CA INDEX NAME)



AB The title reactions give enamines and then N-substituted 1,4-dihydro-4-oxoquinoline-2-carboxylic acids by intramol. cyclization. Ammonia and triethylamine favor cyclization of (pentafluorobenzoyl)pyruvic acid to 2-carboxychromone.

L7 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:295954 CAPLUS
DN 122:132911
TI Reaction of 2-ethoxycarbonyl(carboxy)-5,6,7,8-tetrafluorochromones with N-nucleophiles
AU Saloutin, V. I.; Bazyl, I. T.; Skryabina, Z. E.; Chupakhin, O. N.
CS Inst. Org. Synthesis, Ural Branch Russian Academy Sciences, Ekaterinburg, 620219, Russia
SO Izvestiya Akademii Nauk, Seriya Khimicheskaya (1994), (5), 904-7
CODEN: IASKEA
PB Institut Organicheskoi Khimii im. N. D. Zelinskogo Rossiiskoi Akademii Nauk
DT Journal
LA Russian
IT **161037-54-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with amines)
RN 161037-54-3 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



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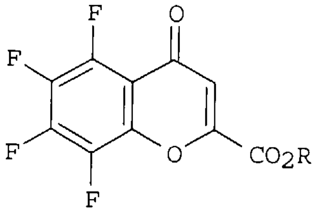
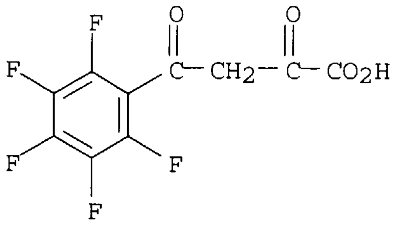


I

AB The direction of reactions of title compds. (I; R = Et, H) with ammonia, methylamine, hexylamine, and aniline depends on the inductive effect of CO2R and on the basicity of the amine. Nucleophilic aromatic replacement of fluorine takes place in the reaction of I (R = Et) with secondary amines (morpholine, N-methylpiperazine) and ethylenediamine.

L7 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:142394 CAPLUS
DN 122:239507
TI Reaction of (pentafluorobenzoyl)pyruvic acid and its esters with N-nucleophiles. Synthesis of 4-oxoquinoline-2-carboxylic acids

AU Saloutin, V. I.; Skryabina, Z. E.; Basyl', I. T.; Kondrat'ev, P. N.; Chupakhin, O. N.
CS Institute of Organic Synthesis, Urals Division, Russian Academy of Sciences, GSP-147, Ekaterinburg, 620219, Russia
SO Journal of Fluorine Chemistry (1994), 69(1), 119-26
CODEN: JFLCAR; ISSN: 0022-1139
PB Elsevier
DT Journal
LA English
IT **162188-41-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with amines)
RN 162188-41-2 CAPLUS
CN Benzenebutanoic acid, 2,3,4,5,6-pentafluoro-α,γ-dioxo- (9CI) (CA INDEX NAME)



AB Nitrogen-substituted 4-oxoquinoline-2-carboxylic acids have been prepared by the reaction of (pentafluorobenzoyl)pyruvic acid (I) with isopropyl-, cyclohexyl-, phenyl-, and 2-hydroxyethylamine. Ammonia and triethylamine, however, reacted with I to form only the 2-carboxy-5,6,7-8-tetrafluorochromone; such behavior has been found in the reactions of Et (pentafluorobenzoyl)pyruvate with ammonia and cyclohexylamine.

L7 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:640906 CAPLUS
DN 119:240906
TI Synthesis and structure-activity relationships of naphthalene-substituted derivatives of the allylamine antimycotic terbinafine
AU Nussbaumer, Peter; Dorfstaetter, Gerhard; Leitner, Ingrid; Mraz, Karin; Vyplel, Hermann; Stuetz, Anton
CS Dep. Dermatol., SANDOZ Forschungsinst., Vienna, A-1235, Austria
SO Journal of Medicinal Chemistry (1993), 36(19), 2810-16
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
IT **110931-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 110931-77-6 CAPLUS
CN Benzenebutanoic acid, 2,4-difluoro-γ-oxo- (9CI) (CA INDEX NAME)